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THE ANATOMICAL BASIS OF THE ARGYLL-ROBERTSON PUPIL.

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We are indebted to Argyll-Robertson, the noted ophthalmological surgeon of Edinburgh, for first drawing accurate attention to the condition of the pupils in diseases of the spinal cord, especially in tabes. He was not the first, however, to notice abnormalities of the pupil in this disease.

Romberg[1] (1851), in his classical description of tabes, after referring to the occurrence of blindness, says: "Even when the optic nerve was not implicated I have repeatedly found a change in the pupil of one or both eyes, consisting of a contraction with loss of motion, which in one case—that of a man, aged forty-five years—attained to such a height that the pupils were reduced to the size of pin-heads." Duchenne, in the 1872 edition of his work (first edition in 1858–59), refers to symptoms that he had long noticed in cases of progressive locomotor ataxia, but to which he had not called sufficient attention, *i. e.*, "the contraction of the pupil, which in these cases is significant, as I have shown, of paralysis of the sympathetic . . . . . usually on one side, but at times on both; it often exists from the onset." He refers to a case in which dilatation of a small pupil occurred during the lightning pains. Nothing was said as to the reflex. This was written after Argyll-Robertson's papers had been published, but, as is well known, the great French describer of new diseases cared but little for the work of other observers, and only read the literature after he had

[1] The Sydenham Society Translations, 1853, vol. ii. p. 397.

written his own description, and even then he seemed to regard it as a rather useless occupation.

Argyll-Robertson's papers were published in 1869, in the February and December numbers of the *Edinburgh Medical Journal*. It is interesting to note that he did not advance the symptom that is so generally called by his name as a sign of locomotor ataxia, but simply as an interesting condition associated with disease of the spinal cord. The first paper is entitled "On an Interesting Series of Eye Symptoms in a Case of Spinal Disease, with Remarks on the Action of Belladonna on the Iris," etc. This was a case of tabes in which there was optic atrophy of the right eye. Both pupils were contracted to a little more than pinpoints—the right eye the smaller of the two. He says: "I could not observe any contraction of either pupil under the influence of light, but on accommodating the eye for a near object both pupils contracted." There was color-blindness of the right eye. Atropine dilated the pupils, and Calabar bean contracted them. The myosis he discusses at some length and explains it by a paralysis of the sympathetic action. He refers to a number of authors who have noted contraction of the pupils in connection with spinal disease. In this paper he does not go into the question of the light reflex, but occupies the rest of the article in discussing the action of atropine and Calabar bean on the iris.

The title of the second article is "Four Cases of Spinal Myosis, with Remarks on the Action of Light on the Pupil." After giving the history of the four cases he says: "In one case the characteristics of locomotor ataxia were well marked; in the other two the form of spinal affection is doubtful; while in the fourth patient, as I have already mentioned, the symptoms of spinal disease are by no means well marked." I think, however, there can be little doubt that they were all cases of tabes, with the possible exception of the fourth. After referring to the first paper he says: "But I now desire to direct special attention to a very remarkable circumstance which I noticed in the case which formed the subject of my previous paper, and which I again observed in all the above cases, viz., that, although the retina is quite sensitive and the pupils contract during the act of accommodation for near objects, yet an alteration in the amount of light admitted to the eye does not influence the size of the pupil." Although in this sentence Argyll-Robertson says nothing about the contracted pupil as being characteristic of the condition he was describing, he did, however, consider it so. It was present in all of his cases, and it was, as we shall see, an important factor in the theory which he advanced as explaining the condition. Since then, however, it has been shown that this peculiar pupillary action, although often, is not always associated with spinal myosis.

Contracted pupils in association with tabes had been pointed out long before Argyll-Robertson's papers, and the new condition that he called attention to is that which he described in the sentence I have quoted above, and it defined accurately what at present is understood as the Argyll-Robertson pupil. This pupillary condition, which Argyll-Robertson advanced simply as a symptom of spinal disease, has become to be regarded as almost pathognomonic of tabes and its allied disease, general paresis, and is universally called by his name. The modern view is well put in the excellent article by Moebius on "Tabes Dorsalis," in the *Twentieth Century Practice of Medicine*, 1897, vol. xi. p. 822. Under the heading "Reflex Iridoplegia," he points out the great importance of the symptom. He considers it the most important symptom of tabes, occurring early and found in about three-fourths of the cases. He states that it is only present in tabes and general paresis, with the exception of extremely rare focal lesions in the region of the corpora quadrigemina.

It would be extremely interesting to follow the fortunes of this symptom from the time Argyll-Robertson was delivered of it to its present assured position in the tabetic hierarchy, in the company of Romberg's symptom, Westphal phenomenon, and Charcot joints. That, however, is impossible at this time, but I should like to mention one or two facts in this connection.

Leyden, in his *Klinik der Ruckenmarks Krankheiten*, 1875, does not refer to it in connection with tabes, but he makes a curious reference in a footnote (vol. ii. p. 176) when writing of acute myelitis. It is as follows: "Argyll-Robertson[1] described another, until then unknown, ocular phenomenon as a result of disease of the spinal cord, to wit, loss of color sense." This would seem to show that he had not looked up the original reference.

As far as I have seen, the symptom was first called after its describer by Dr. T. Granger Stewart, his colleague at Edinburgh. In an excellent article in *Brain* (1879–80, vol. ii. p. 181), concerning "The Eye Symptoms of Locomotor Ataxia," he says (p. 185): "Associated with the myosis, but sometimes occurring independently of it, is another curious feature which was first described in 1869 by Dr. Argyll-Robertson, and which for convenience we are accustomed at the bedside to call the Argyll-Robertson symptom."

That this symptom is an important sign of tabes is so well recognized by all physicians who are interested in the subject that this aspect need not detain us; but as soon as we leave the facts of its occurrence and its importance as a diagnostic sign and try to explain the process which causes it we find ourselves in a maze of conflicting opinions. Argyll-

[1] Edinburgh Medical Journal.

Robertson's explanation is most interesting, and shows clearly the extent of physiological knowledge at that time: "The only possible solution of the difficulty is to be found in the theory that for the contraction of the pupil under light it is necessary that the ciliospinal nerves remain intact, and as in these cases of myosis the ciliospinal nerves are paralyzed, light does not influence the pupil. But hitherto this contraction of the pupil under light has been invariably referred to reflex stimulation of the ciliary branches of the third pair, which supply the circular fibres of the iris. If this latter view were correct I see no reason why in these cases light did not influence the pupils. In all of them the retina was thoroughly sensitive to light, and in all of them the ciliary branches of the third pair were healthy and active (as was shown by the further contraction of the pupil during the act of accommodation, which can only be referred to these nerves); but in all these were symptoms of spinal disease, and in all myosis due to paralysis of the ciliospinal nerves. I am therefore inclined to the former view, in which case it is necessary to assume that the contraction of the pupil, which normally occurs when light is admitted to the eye, is not, as has been hitherto supposed, an excellent example of reflex action, but an isolated example of normal temporary reflex paralysis." Argyll-Robertson was fully aware that the symptoms said to be due to injury of the third nerve (a dilated pupil which was inactive to light) spoke against his theory, but he thought that the cases when reported were not conclusive, and that "for a thorough solution of this question experimental and clinical observations are necessary."

Since that sentence was written numberless clinical observations and many experiments have been made, but the solution of the question is still to be found. The description which Argyll-Robertson gave of the condition has only been changed in that it has been shown that myosis, although a common is not a constant feature, and that the condition is almost exclusively a symptom of tabes dorsalis and dementia paralytica, and not of diseases of the spinal cord in general. Both of these facts must have soon attracted the attention of the distinguished Edinburgh observer, but as far as I have been able to discover he has never published anything else on the subject.

For a thorough solution of the question we must have a complete knowledge of the anatomical and physiological relations which underlie the normal activities of the pupil. Unfortunately, however, our knowledge in these directions is far from complete, as, indeed, in what direction is it not? And in discussing the problem one must often speak with hesitation. However, I shall try to state, as briefly as possible, that which is generally accepted as being true.

First, in regard to the anatomy: The movements of the pupil depend in the end upon the action of the muscles of the iris. The iris has two

muscles, a circular or sphincter muscle, and a radial or dilator muscle. The presence of a sphincter muscle has been unquestioned for a long time, but there has been much dispute regarding the dilator muscle, and it is only very recently that what seems to be definite proof of its existence has been brought. This proof was at first physiological by Langley and Anderson,[1] but later Grunert,[2] after using special methods of bleaching and staining, demonstrated in the human iris a layer of small muscle fibres lying between the stroma and the posterior epithelium. De Vries[3] has studied the embryological development of these fibres, and believes that they are derived from one of the layers of epithelium which cover the ciliary body. Szili[4] has made a similar investigation.

The muscles of the iris are supplied by nerve fibres which enter the posterior aspect of the eyeball through the numerous branches of the ciliary nerve. These branches are derived from two distinct stems. The shorter and more numerous branches come from the ciliary ganglion, which is in close connection with the third nerve, and make up the short ciliary nerves. The other branches are divisions of the long ciliary nerve, which is given off from the nasal branch of the first division of the fifth cerebral nerve. The branches of the long ciliary nerve join with some of those of the short ciliary nerves and enter the eyeball together, and seem to have a similar distribution. It has, however, been shown by physiological experiments that the long ciliary nerve contains the fibres which supply the dilator muscle of the iris, and that the short ciliary nerves are distributed to the sphincter and the ciliary muscles. The long ciliary nerves are made up of neurons which have their cell bodies in the superior cervical sympathetic ganglion. It has been known for a long time that the cervical sympathetic contains fibres which caused dilatation of the pupils; thus as far back as 1727 Petit noted that when the sympathetic was cut the pupil on that side became smaller, and about the middle of the last century a number of experimenters showed that stimulating the cervical sympathetic caused dilatation of the pupil.

Budge and Waller, in papers published in 1851 and later, recorded that if the sympathetic be cut below the superior cervical ganglion the part between the cut and the ganglion degenerated, and that stimulation of it no longer caused dilatation of the pupil; whereas, there were many undegenerated fibres beyond the ganglion, and that stimulation of the ganglion or the nerve beyond caused prompt dilatation. If,

[1] Journal of Physiology, 1892, vol. xiii. p. 554.

[2] Arch. f. Augenheilkunde, 1898; translated in Archives of Ophthalmology, July, 1901, Bd xxx. p. 377.

[3] Nederlandsche Tijdschr. v. Geneesk., 1901, i. p. 194, cited from abstract in Archives d'Ophthalmologie, 1901, Bd. xxi. p. 484.

[4] V. Graefe's Arch. f. Ophthal., 1902, Bd. liii. p. 459.

however, they cut out the ganglion they were unable after a few days to get any dilatation of the pupil by stimulation of the nerve above or of the carotid plexus or of the eyeball itself.[1] Langley, working with colleagues and alone, has, in the course of his illuminating investigations of the sympathetic nervous system, shown that the pupillary dilator fibres run an uninterrupted course from the superior cervical ganglion to the iris. The proof depends largely upon the action of nicotine, for when this drug, in solutions of from 0.5 per cent. to 1 per cent., is applied to a sympathetic ganglion it blocks the transmission of impressions through it, although it does not affect to any extent the conductivity of the nerve fibre. Langley believes this to be due to paralysis of the nerve endings around the cells of the ganglion; that is, a break at the point of contact between the pre-ganglion and post-ganglion fibres.

Now, if the superior cervical ganglion be thus treated with nicotine it is found that stimulation of the cervical sympathetic causes no action; whereas, if the several branches which leave the ganglion above be stimulated, their special functions follow; among these is wide dilatation of the pupil. This is taken to mean that the superior cervical ganglion is a relay station, and gives origin to all the fibres by which sympathetic effects are produced in the head. That these post-ganglionic fibres run without interruption to the peripheral structures, in our case the iris, Langley thinks is indicated by the fact that when nicotine is injected into the general circulation, so paralyzing all the sympathetic ganglia, the effect, in so far as the cervical sympathetic is concerned, is just the same as if nicotine had been applied locally to the superior ganglion—*i. e.*, stimulation below the ganglion produces no effect, while above the fibres are as excitable as ever. The force of this argument depends upon the belief that if these fibres made connection in any other sympathetic ganglion, nicotine would paralyze them at that point and block stimuli applied centrally, although it does not paralyze their endings in the peripheral structures. There are experiments which seem to substantiate this view, and, indeed, to indicate that there are no commissural fibres between sympathetic ganglia.

However this may prove to be, there are other facts which go to prove that there are no ganglion cells interposed in the course of the fibres between the superior cervical ganglion and the dilator muscle of the iris. Schultz[2] has shown that after this ganglion has been cut out and time allowed (eight days) for degeneration of the post-ganglion fibres, cocaine, which in normal eyes and directly after the operation causes dilatation of the pupil, no longer has any effect, which indicates

[1] Budge. Lehrbuch der speciellen Physiol. der Menschen, 1862, Bd. viii. p. 769.
[2] Archiv f. Anat. u. Physiol. (Physiol. Abtheil), 1898, p. 47.

that the degeneration has reached the peripheral endings in the dilator muscle, which would not be the case were another ganglion cell interposed.

Cutting the ciliary nerve back of the eyeball and operations on the eyeball itself have been followed by Nissl changes in some cells in the superior cervical ganglion, which fact speaks for a direct passage of fibres between the structures.[1] The exact course of the fibres from the ganglion to the iris has not been absolutely determined, but is believed to be by the carotid plexus to the Gasserian ganglion and the first division of the fifth nerve, then by its nasal branch to the long ciliary nerve, and so to the iris.

I have stated above that the short ciliary nerves arise from cells in the ciliary ganglion, and are distributed to the sphincter of the iris and the ciliary muscles. This is the commonly accepted view, but it is by no means universally admitted. There has been much dispute over the nature of the ciliary ganglion; that is, whether it is a spinal ganglion and conducts sensory stimuli, as was thought by His, Remak, Van Gehuchten, and others; or whether it is a sympathetic ganglion and conducts motor impulses, as Retzius, v. Michel, v. Koelliker, among others, have held. Bach[2] and Marina[3] have given good reviews of the subject, where references to the literature can be found, as well as a description of their own experiments. The difference of opinion has been due to the variety of methods used in attacking the problem and the fact that animals of different species were employed by the different observers. Langley and Anderson,[4] experimenting with nicotine, found that this ganglion stood in the same relation to the pupillary fibres running in the third nerve that the superior cervical ganglion bore to the analogous fibres of the cervical sympathetic; for if nicotine be applied to the ciliary ganglion, stimulation of the third nerve no longer causes contraction of the pupil, although stimulation of the ciliary nerve does. Marina got similar results by injecting nicotine into the orbit. If the third nerve be cut[5] degeneration can be traced up to but not beyond the ganglion. Injury to the iris or cutting of the ciliary nerve is followed by Nissl changes in the cells of the ganglion (Bach, Marina, Bumm[6]). These facts can only be interpreted by the belief that the ciliary ganglion is, at least in part, a sympathetic ganglion, and gives origin to the fibres which supply the sphincter muscle of the iris and the ciliary muscles. These fibres are sympathetic, post-ganglionic fibres, and are for the most part non-medullated. When

[1] Marina. Deutsche Zeitschrift f. Nervenheilkunde, 1899, Bd. xiv. p. 357.
[2] Von Graefe's Arch. f. Ophthal., 1899, Bd. xlvii. pp. 339-551.
[3] Deutsche Zeitschrift f. Nervenheilk., 1899, Bd. xiv. p. 357; 1901, Bd. xx. p. 369.
[4] Journal of Physiology, 1892, vol. xiii. p. 460.
[5] Apolant. Arch. f. mikrosk. Anat., 1896, Bd. xlvii. p. 655.
[6] Neurol. Centr., 1902, Bd. xxi. p. 423.

we remember that these muscles are composed of smooth muscle fibres, which have developed from epithelium, we are not surprised at this arrangement, for it would be a unique occurrence should such muscles be supplied directly by a cerebrospinal nerve.

The ciliary ganglion seems to be a more complicated structure and to be connected with other nerves besides the third. Dissection shows that it is connected by a filament with the ophthalmic branch of the fifth, and that it also receives a root from the sympathetic by the cavernous plexus. Histological examination shows that the ganglion contains cells of various character, and that there is quite a variation in this regard between animals of different species.[1] Marina found that by destroying the cornea and so injuring the endings of the fifth nerve, a subsequent examination of the ciliary ganglion by Nissl's method showed that certain of its cells had undergone degenerative changes. After iridectomy there were a greater number of degenerated cells. This degeneration was still greater if the eyeballs were eviscerated, and greatest of all when the ciliary nerves were cut. He found in monkeys, together with the degeneration in the ciliary ganglion, degenerated cells in the Gasserian ganglion and less evidently in the superior cervical sympathetic ganglion. Bach[2] got slightly different results, as he was unable to find any degenerated cells when the cornea was alone injured, whereas if he removed the iris and ciliary bodies he got degeneration in practically all of the cells. Both these writers appear to consider the ciliary ganglion as a mixed ganglion, containing both sympathetic and spinal cells. Bernheimer, experimenting in the same manner, thought that he got evidence that the ganglion was almost entirely spinal. Marina states that in monkeys the proportion is seven-eighths sympathetic and one-eighth spinal. The latest investigation of this subject is one by Bumm,[3] but as yet I have only seen an abstract of the paper which he read before a society of alienists in April of last year. His investigation was particularly to find out the character of the cells which did not degenerate after the cutting of the ciliary nerve. He counted the number of ganglion cells which were normally present in a ciliary ganglion, and found the average to be 6432. After cutting the ciliary nerves there were left 3845 unaffected cells. He also cut out the superior cervical sympathetic ganglion and found that the cells were then reduced to 2587. The nature of these remaining cells is undetermined; they are too numerous to be simply connecting cells (Schaltzellen). There are some T-shaped cells which he thinks belong to the fifth nerve, and he says that perhaps the others are to be brought into connection with the intraorbital ganglion, which has been lately described.

[1] Marina. Deut. Zeitsch. f. Nervenhk., 1899, Bd. xiv. p. 357.
[2] Von Graefe's Arch. f. Ophthal., 1899, Bd. xlvii. [3] Neurol. Contr., 1902, Bd. xxi. p. 423.

The pre-ganglionic fibres which carry impulses to the pupillary fibres from these two ganglia—the superior cervical sympathetic and the ciliary—have also given rise to a good deal of controversy. Those which run to the superior cervical ganglion are, perhaps, better known.

Budge, in the middle of the last century, showed that they left the central nervous system from the lower part of the cervical and upper part of the thoracic cord. He determined this by direct stimulation of the cord itself, and stimulation of the roots as they left the intervertebral ganglia. It was in this region of the cord that Budge placed his "inferior ciliospinal centre." He also assumed a higher centre which he placed near the hypoglossal nerve, but he seems to have based his belief in this on anatomical rather than experimental grounds. This question has been studied by a number of investigators. Among the later ones I may mention Madame Dejerine, Langley, and his associates. Langley believes that the pupillary fibres leave the cord by the first, second, and to some extent the third thoracic roots. His experiments with nicotine show that the fibres run through the lower cervical ganglia, to end about the cells in the superior cervical ganglion. These pre-ganglionic fibres are fine, medullated fibres, and arise from cells somewhere within the central nervous system. It is believed that the cells of origin of fibres running to the sympathetic system in general lie in or near the segment from which the fibres leave the cord, and Gaskell thinks that they are to be found in the lateral column of the cord. There is, however, no very conclusive proof of this.

It was about the middle of the last century that physiologists showed that the third cerebral nerve contained pupillary constrictor fibres. I do not know who first made this observation, but Romberg, in his text-book on *Nervous Diseases*, refers to dilatation of the pupil as a symptom of paralysis of the third nerve, and Budge,[1] in his *Physiology*, speaks of contraction of the pupil which followed stimulation of the third, in recently killed animals and man. Argyll-Robertson, in 1869, did not feel that this point was definitely proved, and explained the contraction of the pupil to light by inhibition of the ciliospinal (dilator centre); and very lately Marina, from a study of the cases of ophthalmoplegia, believes that he has found evidence that the third nerve may be severely injured without causing paralysis of the sphincter of the iris. He explains this not by denying that the third nerve contains pupillary fibres, but by the assumption that the ciliary ganglion is the chief reflex centre for the iris. However, there can be little doubt that the third nerve does contain these fibres, and that they represent the pre-ganglionic fibres of the ciliary ganglion. The principal question in dispute is as to the position of the cell bodies from which they arise.

[1] Ibid., p. 805.

One would naturally look for them in or near the nucleus of the third nerve, and Bernheimer seems to have determined in just which group of the cells of the nucleus they are to be found.

The third nucleus is a complicated collection of nerve cells lying ventrally to the aqueduct of Sylvius, at the level of the corpora quadrigemina, and has been more or less accurately divided into smaller groups of cells which are believed to bear definite relations to the several muscles supplied by the third nerve. Bernheimer's work has been particularly valuable in this connection. He, as well as other investigators, has shown by the use of the Nissl method that there are two collections of cells within the third nucleus which do not seem to bear any relation to the external muscles of the eye. These are in the anterior part of the nucleus, and occupy a medial position; and he designates them as the large-celled, unpaired, median nucleus; and the small-celled, paired, median nucleus. This nucleus is practically the same group of cells which we have been accustomed to call "the nucleus of Edinger-Westphal."

In a brilliant experimental work Bernheimer[1] has proved that if this small-celled, paired median nucleus be injured the sphincter of the iris is paralyzed. He operated on six monkeys, but was successful in destroying this group of cells in only one case. In this animal the pupil was dilated and did not react to light. The brain of this, as well as that of the other animals, was most carefully examined, and serial sections made, and it was shown that it was in fact this special nucleus that was injured in the one animal; while in the other five, in whom the pupils were perfectly normal, it had not been touched. Whether or not the pupil was also paralyzed during accommodation seems not to have been determined, but it is probable that this movement is represented in close connection with the reflex movement of the iris, possibly in the large-celled, unpaired, median nucleus.

In this very brief review I have endeavored to trace what is known of the path by which the motor influences governing the iris leave the central nervous system and reach the eye; and I believe that we may state as the best substantiated view the following conclusions: The sphincter and dilator muscles of the iris are composed of smooth muscle fibres, and are each controlled by sympathetic nerve fibres. As is true of the sympathetic nervous system in general, the path from the central nervous system to the periphery is made up of two sets of nerve fibres—the so-called pre-ganglionic and the post-ganglionic fibres. The pre-ganglionic fibres, which control the sphincter muscle of the iris, arise from a definite group of cells in the anterior part of the nucleus of the third nerve, and run to the ciliary ganglion. From this ganglion the

[1] Von Graefe's Arch. f. Ophthalmologie, 1901, Bd. lii., Heft ii. p. 302.

post-ganglionic fibres arise and are distributed through the short ciliary nerve to the sphincter muscle. The path controlling the dilator muscle is a longer and more complex one. Its pre-ganglionic fibres arise from cells in the spinal cord, which are probably situated in the lateral horns, about the level of the junction of its thoracic and cervical portion. The fibres leave the cord mostly by the first thoracic nerve and run in the cervical sympathetic to the superior cervical ganglion. From this structure post-ganglionic fibres arise, which, after a somewhat circuitous route, reach the eye and the dilator muscle of the iris through the long ciliary nerves.

The afferent path of the reflex arc, which governs the action of the pupil to light, is also not absolutely determined. The impulses start in the retina, and in general are provoked by the same sort of stimuli that give rise to visual impressions. It was at first assumed that the visual and reflex fibres were the same, and that the paths only separated beyond the primary optical centres, but later observations seem to indicate that the reflex fibres and the visual fibres are not identical. As is known, the fibres of the optic tract run to three nuclei and are believed to end there, about the cells which are contained in them. These nuclei, which are the so-called primary optical centres, are the lateral geniculate body, the anterior corpora quadrigemina, and the pulvinar of the optic thalamus. There is considerable variation in animals of different species as to the relative number of fibres which run to each of these nuclei. In man, Bach[1] states, most of the fibres end in the geniculate body, and the smaller number run to the two other structures. The anatomical relation of the anterior pair of the corpora quadrigemina to the nucleus of the third nerve has led most observers to assume that it was in this structure that the afferent limb of the pupillary reflex arc ended, and that its gray matter was connected by comparatively short fibres with the nucleus of the third nerve. Von Bechterew and others, experimenting on the corpora quadrigemina, found that in certain animals injury to this structure did not cause disturbance of the light reflex, and it was these experiments that first led to the supposition that the reflex fibres in the optic tract were distinct from the visual fibres.[2] The endeavor to determine the course of these reflex fibres has given rise to a great deal of interesting experimentation, but it must be acknowledged that there is no definite proof in regard to their existence. We do not know from what special cells in the retina they arise. But we do know that the reflex path runs in the optic nerve to the chiasm, where there is a partial decussation, and it seems fairly certain that those fibres which arise from the temporal half of the retina do not, for the most part, decussate, but continue in the optic

[1] Bach. Deut. Zeitschr. f. Nervenhk., Bd. xvii. p. 428.
[2] Von Bechterew. Ibid., 1900, Bd. xvi. p. 194.

tract of the same side. During their course in the tract the direct and crossed fibres seem to be pretty well intermingled. There is much discussion as to just the point at which the pupillary fibres leave the optic tract. Von Bechterew[1] states as his present view that they leave the tract at the level between the corpus cinereum and the root fibres of the third nerve—*i. e.*, near the place where the optic tract enters the geniculate body—and run to the posterior part of the third ventricle, where they apparently make new connections before they run to the nucleus of the third nerve.

Bernheimer[2] concludes from his embryological examination and from the experiments which he made on monkeys that the pupillary fibres leave the optic tract just before they reach the external geniculate body, and run toward the middle line within the white matter of the corpora quadrigemina, where they turn, some going to the gray matter of this structure and others directly to the region of the sphincter centres in the third nucleus.

Bach,[3] working in the laboratory of Prof. v. Michel, was unable to confirm Bernheimer's results. He experimented on pigeons, rabbits, cats, and monkeys, and could find no evidence, either from his own work or from a review of the literature, for the occurrence of a direct passage of fibres from the optic tract to the nucleus of the third nerve. He believes that Bernheimer's statements are due to a misinterpretation of his findings. Bach's results are practically in accord with those of most other investigators who have worked on this point, and he points out that it would be a unique circumstance to find afferent fibres ending directly about motor cells without the intervention of connecting cells. In this he does not take into account the complicated structure of the retina. The disagreement seems largely to be due to the different interpretations which the several observers have given to the picture obtained by the more delicate histological methods, particularly those of Marchi and Nissl.

Bernheimer's view is so simple and direct, and, backed as it is by such an authority, that one is naturally very much attracted to it. It assumes that the reflex arc, upon which the contraction of the pupil to light depends, is of the simplest nature. The afferent limb is made up of the pupillary reflex fibres, which arise in the retina, partially decussate in the chiasm, and run directly to the sphincter centre of the third nucleus, the centre on each side receiving fibres from both optic tracts, and being mutually connected with each other. The efferent limb is composed of fibres which arise in the sphincter centre and run directly to the sphincter muscle of the iris without making connection

[1] Loc. cit. [2] Von Graefe's Arch. f. Ophthalmologie, 1899, Bd. xlvii. p. 1.
[3] Deut. Zeitschrift f. Nervenhk., 1900, Bd. xvii. p. 428.

with the ciliary ganglion or elsewhere. Other authors, however, have brought forward what they believe to be evidence that the pupillary reflex fibres end in a number of different structures, among which may be mentioned the anterior pair of the corpora quadrigemina, the pulvinar, the corpus Luys, the ganglion habenula, and the gray matter about the third ventricle. Whatever the ultimate solution of the question may be, the data which we have at present is too incomplete and conflicting to allow us to accept any of the present views as final. All that one can now say is that if these fibres do not end as Bernheimer believes we do not know how they end.

Pathological examinations and direct experiments have been used to throw light on the position of this reflex arc, and I have already referred to the experiments of v. Bechterew and others, which seem to indicate that the corpora quadrigemina has little, if anything, to do with the light reflex, and those of Bernheimer, which he takes as establishing the position of the pupillary centre in the third nucleus, and I shall refer below to some very recent experiments bearing on the question; but first there are some interesting pathological observations that must be considered.

Argyll-Robertson described the pupillary condition which bears his name as a symptom of a disease of the spinal cord, and the explanation which he gave depends upon the assumption of a lesion in the cilio-spinal centre of Budge. But soon afterward attention was directed to the third nucleus and the region near it, and it is about this area that the discussion was waged. Certain investigators, however, kept their attention fixed on the spinal cord; and Rieger and v. Forster, in 1881, tried to show that the ocular symptoms of tabes and general paresis were due to lesions of this structure. Their articles attracted very little attention at the time of its publication, and it was not until very lately that the work of Wolff and Bach aroused new interest in this phase of the subject. Wolff[1] gives an analysis of the cases which Prof. Rieger had collected up to that time. These are cases of general paresis and tabes which had come to autopsy. He concluded from them that whenever there is a loss of the light reflex there is also a lesion in the upper part of the cervical cord. He gives no theory as to just where the centre is, nor as to its connections. In a second article Wolff[2] reports an interesting case in which the Argyll-Robertson pupil occurred, and in which, among other things, a gumma was found in the posterior columns of the spinal cord at the level of the second and third cervical roots. The region of the third nucleus was apparently free. This case Wolff justly thinks is, to say the least, suggestive.

[1] Arch. f. Psych., 1899, Bd. xxxii. p. 57.

[2] Deut. Zeitschr. f. Nervenhk., 1902, Bd. xxi. p. 247.

A recent case reported from Rieger's clinic by Reichardt[1] is of interest in this connection as it is somewhat contradictory. He examined the central nervous system of a man, aged twenty-one years, who had had congenital immobility to light of his pupils. Whether the pupils had also been immobile during accommodation had not been determined, on account of the patient's mental condition. There was no lesion that could be demonstrated in the cervical cord, where Wolff, who had also seen the case, expected to find one; nor was there a lesion found anywhere else that might explain the condition, but, unfortunately, the region of the third nucleus was spoiled in preparation and could not be examined.

Bach[2] also, under the inspiration of Prof. Rieger, undertook some experiments to determine this point. He cut off the heads of cats, albino rabbits, and monkeys, making the knife pass as near the skull as possible, and at once tested the pupillary light reflex. He found that the reflex was present and remained so at times for two months. There was, however, two or three centimetres of the spinal cord left; so he altered his experiments so that he destroyed this remaining part of the cord immediately after the decapitation. After this procedure the reflex was abolished at once. From these experiments he concluded that the centre for the light reflex was to be looked for in the cervical cord, just below the medulla. His extensive anatomical investigations gave him no definite clew as to the connections of this centre, but in his next paper[3] he gives his reasons for thinking that it may be connected with the primary optical centres by the lemniscus and with the nucleus of the third nerve by the posterior longitudinal bundle.

In some of the later works on diseases of the nervous system the view that the centre for the light reflex is to be found in the cervical cord has been accepted, and notably by Sacki and Schmaus,[4] and Schaffer.[5] Ruge[6] repeated Bach's experiments, and confirmed the result that after decapitation and removal of the remaining spinal cord the reflex was at once abolished. He noticed, however, that the size of the pupil varied greatly in the different animals experimented upon. In one they might be contracted and in another dilated, and in the mid-position in a third. From this he concluded that there must be some secondary action taking place to which the loss of the light reflex might be due. He then succeeded in cutting at the level of the calamus scriptorius and as high as the middle of the fourth ventricle, and he always found the light reflex to be present after these

[1] Neurologische Centralblatt, 1903, Bd. xxii. p. 521.
[2] Von Graefe's Arch. f. Ophthal., 1899, Bd. xlvii. pp. 339 and 551.
[3] Deut. Zeitschr. f. Nervenhk., 1900, Bd. xvii. p. 428.
[4] Vorhsungen u. d. path. Anat. der Rucherenecke, 1901.
[5] Anatom. klin. Vorträge an dem Geberte d. Neuropathol., 1901.
[6] Von Graefe's Arch. f. Ophthal., 1902, Bd. liv. p. 483.

procedures, just as it had been when the cut was made in the spinal cord, and this he takes as proving that the centre is in the brain. In spite of this he thinks that the Argyll-Robertson pupil may be accounted for by a lesion in the cervical cord, and his hypothesis suggests so strongly the explanation which Argyll-Robertson originally gave that it is of special interest in this connection. He refers to the fact that the pupillary fibres of the third nerve end about cells in the ciliary ganglion and reach the iris through sympathetic fibres. He believes that it is not unreasonable to think that a lesion in the spinal cord at the level of the exit of the fibres going to the cervical sympathetic would produce such an effect on the sympathetic cells of the ciliary ganglion that they could no longer transmit the impulses received through the third nerve and so interrupt the reflex arc. Ruge gives no explanation of how such an effect could occur, nor does he seem to have taken into consideration the many experiments which have been done on the sympathetic nervous system.

Bach, together with Meyer,[1] has reported some additional experiments, the results of which have led him to modify his former view. These authors did not know of Ruge's work until their own experiments had been finished. They used the apparatus which Meyer had devised for maintaining artificial respiration, and were thus able to observe the animals for a considerable time. They used full-grown cats, and found that section of the cervical cord 1 mm. or 2 mm. below the medulla caused no loss of the pupillary reflex, but that if the cut passed just at the spinal end of the fourth ventricle the reflex was abolished. If the section were unilateral it was the reflex of the opposite eye which was lost. Bach and Meyer suppose that in this region there is a centre of great importance for the pupillary light reflex. They consider that it is an inhibitory centre, for when the medulla and fourth ventricle are simply exposed the pupils become contracted and react very little, if at all, to light, presumably from irritation of this centre, and if then a cut be made in the middle of the fourth ventricle, or even above, the pupils again become about the normal size and react actively to light. This is equally so in both eyes, even when the cut is unilateral. They believe that there must be another centre for the light reflex—a subordinate centre which is situated not below the posterior corpora quadrigemina. They give an elaborate diagram, which is a modification of the one which Bach had already given. In this they leave it an open question whether the third nucleus plays any part in the reflex act or whether the efferent path is not composed of fibres which run directly from the two centres to the ciliary ganglia. They believe that the efferent path decussates, at least for the most part, and passes

[1] Von Graefe's Arch. f. Ophthal., 1903, Bd. lv. p. 414.

to the eye of the opposite side, and that there is no connection between the reflex centres of the two sides. The afferent path, after having decussated in the chiasm, passes, they believe, only to the upper reflex centre of the same side, and that the path from there to the inhibitory centre is also direct. In their account of symptoms which follow lesions in the various parts of this complicated reflex mechanism they do not indicate where we are to look for the lesions which underlie the Argyll-Robertson pupil. Bach and Meyer[1] have added the report of some more elaborate experiments along this same line. They exposed the medulla and stimulated mechanically the floor of the fourth ventricle, and were able to produce changes in the size and action of the pupils which spoke for the presence of their inhibitory centre and also for the presence of the centre which has to do with the dilatation of the pupil, probably also inhibitory. They cut out the medulla and allowed the animals to become asphyxiated, when the pupils dilated ad maximum, to again contract when artificial respiration was recommenced. Electrical stimulation of cerebral cut surfaces caused dilatation. From this they conclude that there are other parts of the central nervous system which are important for pupillary dilatation. Their experiments, as well as those of Rieger, show that a lesion of the upper part of the cervical cord can hardly be held accountable for the symptoms unless it does so through the agency of the ciliospinal nerve. This is Rieger's supposition, and what Argyll-Robertson believed.

While practically all observers have assumed that the lesion underlying the Argyll-Robertson pupils was to be looked for in the central nervous system, Marina[2] has called particular attention to the importance of the ciliary ganglion as a centre for the pupillary light reflex. I have already referred to his careful anatomical and experimental studies, which have done much to make our knowledge of this ganglion more accurate. He has also examined the ciliary ganglion in various pathological conditions, and he gives the results of his findings in seventy cases. Among these were thirty-six cases of *dementia paralytica*, five of *tabes*, and twenty-nine of other diseases. He seems to have fully recognized the difficulty in the interpretation of Nissl changes, and to have endeavored to control his findings. His conclusions are that in *dementia paralytica* and in *tabes*, when the pupils have reacted normally during life, no changes are to be found in the ciliary ganglion after death; but that when there has been an abnormal pupillary reaction there will be found more or less evident changes in the cells of this ganglion. The changes indicate, he thinks, a slowly progressing degeneration of the cells. He also finds degeneration of the

[1] Von Graefe's Arch. f. Ophth., 1908, Bd. lvi. p. 297.
[2] Deut. Zeitschr. f. Nervenhk., 1901, Bd. xx. p. 369.

ciliary nerve particularly well marked in the cases of tabes. No change in the third nerve or its nucleus was found.

In a number of cases Marina examined the superior cervical sympathetic ganglion, and although his results were not so definite as in the case of the ciliary ganglion, it did seem to him that when the pupils were normal and no changes were found in the ciliary ganglion there were little or no changes in the superior cervical ganglion. He, however, does not mean to draw a parallel between these two organs.

Marina was unable to determine a constant microscopic difference in the ciliary ganglion between the cases with Argyll-Robertson pupils and those in which the pupils were completely immobile, but he calls attention to the fact that in the great majority of cases there were some normal cells remaining. He speaks of the complexity of the problem and of the many undetermined factors in regard to the action of the pupil during convergence and accommodation. In a very recent paper[1] he has studied experimentally the contraction of the pupil during convergence, and he believes he has proved that the action is entirely independent of the third nucleus. He transplanted the rectus internus into the insertion of the superior oblique and into that of the rectus externus, in several monkeys, and found that wherever the eyes were converged without relation to the muscle which brought about the position the pupil contracted. He suggests as a possible hypothesis that the contraction may be caused by stretching of the short ciliary nerves, and so stimulating the ciliary ganglion and causing a contraction of the pupil this way.

Although he admits the presence of other reflex centres for light, Marina insists upon the importance of the ciliary ganglion, and he predicts that the oftener it is examined and the more it is studied in his relation the greater this importance will become. This work is very interesting just now, when more attention is being paid to the sympathetic ganglia as possible reflex centres, and one is reminded of the work of Müller[2] and others, which seems to show that the reflex activities of the bladder are largely under the control of the sympathetic ganglia in its neighborhood. The mechanism which controls the bladder and that which controls the iris have many points of analogy, and it is interesting to remember how often they are both disturbed in the early stages of tabes.

Suggestive as all this undoubtedly is, it cannot be said to be anything more, for our knowledge of the sympathetic nervous system is far too incomplete and inexact to allow us to formulate any clear idea of how the ciliary ganglion could act as a reflex light centre. Marina

[1] Deutsche Zeitschrift für Nervenheilkunde, 1903, vol. xxiv. p. 274.
[2] Ibid., 1901, Bd. xxi. p. 86.]

advances no theory. If I have understood Langley,[1] who appears to have the clearest conception of the sympathetic, or, to use his more general term, autonomic nervous system, he would believe that such a function of the ciliary ganglion would not be in accordance with what is at present known.

A CONTRIBUTION TO THE SURGERY OF CEREBRAL TUMORS.

By George Woolsey, M.D.,
of New York City.

The reaction which followed the indiscriminate resort to operation for cerebral tumors, which was stimulated by the publication of the successful cases by Godlee and Horsley, has led to an ultra-conservative attitude toward the operation by most surgeons. Operation in cases imperfectly localized naturally produced discouraging results.

At the outset we must admit that only a small proportion of all cases of cerebral tumor are suitable for radical operative treatment—a proportion which varies from 2 to 8 per cent., according to various neurologists, judged on the basis of the autopsy findings, or runs up to 16 per cent., judged by the histories of those clinically diagnosed. According to Starr, about 7 per cent. of all cases are operable. This small percentage depends largely on our imperfect means of exact diagnosis and localization and on the inaccessibility of certain parts of the brain to successful surgical operation. With the improvements in the methods of cerebral localization and in technique the operation has become safer, its indications have been extended, and the proportion of operable cases is likely to increase to a certain extent. The fact should not be lost sight of that all cases of brain tumor, of whatever variety, are necessarily fatal.

The conservative attitude referred to is illustrated by v. Bergmann, one of the highest authorities on brain surgery, who would limit the surgery of brain tumors to those of the central or motor area, on the ground that an exact diagnosis is possible only in tumors of or near this region. V. Bergmann himself, however, operates on tumors in other regions, as his published cases show, and the unfortunate outcome of many of these cases may be a factor in his ultra-conservatism. My own experience in operations on cerebral tumors and cysts—three for tumors and two for cysts—and my interest in cerebral localization induced me to collect the cases of cerebral tumors operated on (including cysts giving the symptoms of tumor), which have been reported during the past five years (101 cases), with a view to determine whether the results of the more recent operations on cerebral tumors do not

[1] Brain, Spring, 1903.

justify a less conservative attitude toward their operative treatment. In this list I have included only those cases reported in the English, French, German, and American literature with sufficient fulness to furnish the data required. Of my own cases two have been shown to the New York Surgical Society, and published in the *Annals of Surgery*, February, 1903, p. 276, to which reference may be made for details. Similar collections of cases have been made by Knapp, Starr, v. Bergmann, and others up to 1898. The cases reported in the five years since then would indicate whether the improvements in localization and technique justify us in extending the indications as given by v. Bergmann and in taking a more hopeful view of the surgery of cerebral tumors.

As for cerebral tumors in that part of the cerebral cortex accessible to surgical operation, the indications for operation depend entirely upon the possibility of accurate localization. What light does this series of 101 cases show as to this point? I think it shows that, in many cases at least, tumors of the prefrontal, parietal, and occipital areas can be as successfully localized and operated upon as those of the motor area. In this series of 101 cases twelve were localized in the frontal region, four of which really belonged to the motor area, including the posterior parts of the second and third frontal gyri. The remaining eight cases (Nos. 11, 43, 71, 72, 73, 75, 77, and 82) were situated in the prefrontal region, and present quite a characteristic group of symptoms for aid in local diagnosis. This area, especially that on the left side, is supposed by many to have to do with the higher psychic powers and the moral sense. From the analysis of 775 cases of brain tumor accompanied by psychic disturbances, Schuster[1] claims that certain psychic symptoms correspond to certain forms and groups of anatomical and local conditions, and that frontal tumors present moral insanity and dementia—and less often hallucinations, paranoia, and mania—more often than tumors elsewhere. Gianelli[2] says that the more prominent the psychic disorders—torpor, weak memory, etc.—the more likely is the growth to be in the prefrontal lobe, and that seventy-seven out of ninety-seven cases of tumor of the frontal lobe were accompanied by mental disturbance. All of the above eight cases of frontal tumor, irrespective of the side, show psychic symptoms, and two of them moral perversion. L. Bruns[3] says that disturbance of equilibrium characterizes tumors of both the frontal lobe and the cerebellum, but a distinct ataxic gait was present in only one of the above eight cases. To assist in the localization, three presented local tenderness on pressure or percussion, one a visible external swelling, two exophthalmos, and in two the eye was lowered and turned out.

No.	By whom and where reported.	Sex and age.	Choked disk.	Headache.	Position.	Variety.	Operator.	Recovery.	Cure.	Improvement.	Deaths.	Remarks.
1	Oliver and Williamson. Brit Med. Journ., Nov. 26, 1898.	M. 34	+	+	R. motor area.	Small round-celled sarcoma.	Williamson.	+	+	...	...	1½ years later, apparent slight recurrence.
2	Ibid.	F. 23	+	+	L. motor area (lower part).	Angioma.	"	+	...	+ great.	...	Only paresis of hand remained.
3	K. Bonhoeffer. Monats. f. Psych. u. Neurol., 1898, iii. 297.	M. 28	+ late.	+	R. motor area (anter. part).	Glioma.	Mikulicz.	+	...	+	...	Recurrence; death in three months.
4	Ziehen. Zeits. f. prakt. Aerzte, 1898, 113.	M. 45	—	—	L. motor area.	Fibrosarcoma.	Riedel.	+	...	...	2d wk	Death from meningitis.
5	Haasler. Archiv. f. Psychiatrie, 1898, xxx. 660.	M. 29	+	+ r. side.	R. motor and front. region.	Spindle-celled sarcoma.	v. Bramann.	+	...	+ great.	...	Shown 5½ years later; no recurrence.
6	Nedwill. Lancet, 1898, p. 1466.	F. 17	+ right.	+	R. motor area.	Hydatid cyst.	Nedwill.	+	...	+	...	
7	Kosinski. Medycyna, 1898, pp. 1-5.	M. 26	+ right.	+	" "	Angiosarcoma	Kosinski.	+	...	+ great.	...	
8	v. Friedlander und Schlesinger. Wien. klin. Woch., 1898, No. 4.	M. 43	+	+	L. motor area inf. and ant.	Gumma of dura.	Albert.	+	...	+ great.	...	Nearly a cure.
9	Schlesinger. Ibid.	M. 23	?	?	R. motor area.	Fibroma.	"	+	...	+ great.	...	No recurrence 8 years after.
10	Ibid.	M. ?	+ late.	+	" "	Gliosarcoma.	Ewald.	+	...	+	...	Symptoms returned in five months; death 6-7 mos.; r. hemisphere infiltrated.
11	Thomas and Keen. Year Book of Med. and Surg., 1898, pp 410 and 719.	M. 17	+ left.	—	2d l. frontal convolution.	Sarcoma.	Keen.	+	...	great.	...	Tumor subcortical; lateral ventricle opened and drained.
12	W. C. Krause. New York Med. Jour., July 30, 1898.	M. 45	+ late.	+ r. side.	R. motor area.	Small round-celled sarcoma.	R. G. Wilcox.	+	...	...	14 days.	Temporary improvement; multiple tumors found.
13	Ibid.	F. 42	+ right.	+	L. motor area.	Glioma.	"	+	...	...	19 days.	Death from pneumonia.
14	Ibid.	M. 40	+ double.	+	R. motor area.	?	.....	+	...	+	...	Left hospital in 8 months.
15	Crowley. Trans. Med. Soc., California, 1898, p. 202.	F. 42	?	—	L. motor area.	Fibrosarcoma.	Stratton.	+	...	+	...	Recurrence; second operation in 9 months; death a few days later.
16	Grisson. Neurolog. Centralbl., 1898, p. 1138.	M. 27	—	+	L. motor area (post. part).	Cyst.	Grisson.	+	+	...	...	
17	S. E. Henschen. Mittheil. a. d. Grenzgebiet d. Med. u. Chir., 1898, No. 3.	M. 45	—	?	L. motor area.	Cystoglioma.	Lennander.	+	...	+	...	Cyst partly extirpated; repeated recurrences and operations. Death in 8 months.
18	Ibid.	M. 45	+	+	R. motor area.	Spindle-celled sarcoma.	"	+	...	+	...	Death 3 years later; hemorrhage caused operation to be suspended.

19	Willy Meyer. Ann. of Surg., 1898, xxvii. 770.	M. 30	+	+	R. motor area.	Cyst.	Meyer.	+	...	+	...	Hernia cerebri; skin grafted; report 4 months later.
20	A. Wiener. New York Med. Journ., Oct. 15, 1898.	M. 20	+	+	L. motor area.	Glioma.	Gerster and Lilienthal.	+	...	+	...	Recurrence; condition hopeless; operation in two stages for hemorrhage.
21	J. M. Nicholl. Lancet, Oct. 29, 1898.	M. 12	+ right.	+ r. side.	R. petrous bone pressing on r. temp. sph. lobe.	Alveolar sarcoma.	Nicholl.	+	...	+	...	Recurrence; death in 2½ months; removal incomplete.
22	Gordinier. Albany Med. Annals, Sept., 1898.	M. 49	+	+	R. motor area.	Small round-celled sarcoma.	Seymour.	+	...	+	...	Tumor subcortical in centrum ovale; none seen or felt at operation.
23	Pearce Gould. Clin. Soc. Trans., 1898, xxxi. 286.	M. 41	—	+	?	?	Gould.	+	+	...	...	Was there a tumor? none found.
24	Liepmann. Monatschr. f. Psych. u. Neurol., 1899, iii. 407.	F. 32	—	+	?	?	Kolaczek.	+	...	—	...	No improvement; was there a tumor? none found.
25	Adenot and Carrier. Archiv. provincal de Chir., 1898, p. 154.	F. 11	—	—	L. motor area, upper third.	Glioma.	.....	+	...	—	...	Worse rather than better.
26	E. Hitzig. Mitth. a. d. Grenzgeb. d. Med. u. Chir., 1898, iii. 367.	M. 48	—	—	R. motor area, middle third.	Cyst.	.....	...	...	...	24 hours	
27	Seydel. Münch. med. Woch., 1898, Nos. 9, 10.	M. 47	+	+	L. motor area.	Fibroma of dura.	Seydel.	+	+	...	...	Recurrence; second operation; death in 2½ years; operation in two stages.
28	Putnam & Richardson. Boston Med. and Surg. Journ., Feb. 9, 1898.	M. 38	+	+	" "	Sarcoma.	Richardson.	+	...	+	...	Death 7 mos. after second operation, 10 mos. from first; tumor subcortical.
29	Gordinier. Amer. Journ. of Med. Sci., May, 1899.	F. 37	+	+	2d l. frontal convolution.	Glioma.	E. D. Ferguson	...	...	...	+	Agraphia and no aphasia.
30	J. M. Ball. Phil. Med. Journ., Oct. 28, 1899.	M. 57	double.	...	R. operculum and insula.	Spindle-celled sarcoma.	Lamphear.	...	...	...	few hours	Insufficient data for localization; operation on wrong side.
31	Bayerthal. Münch. Med. Woch., 1899, No. 46.	M. 29	—	—	R. paracentral lobule.	Solitary tubercle.	Heidenhain.	+	...	+ great.	...	Report 1 year later; operation in two stages; tumor subcortical.
32	R. Haas. Beiträge z. klin. Chir., 1899, p. 601.	M. 41	—	+	R. motor area, upper ¼.	Spindle-celled sarcoma.	Czerny.	+	+	...	...	
33	Ibid.	F. 18	+	+	?	?	"	+	...	...	+	Death 10 days after second operation; nothing found.
34	Ibid.	M. 5	?	?	?	?	Jordan.	+	...	+	..	Nothing found.
35	Ibid.	M. 55	—	+	R. motor area.	Round-celled sarcoma.	Czerny.	...	...	...	+	
36	Handford. Brit. Med. Journ., March 11, 1899.	M. 19	+	+ r. side.	" "	Osteoma.	Anderson.	+	...	+	+	
37	Bramwell. Clin. Journ., 1900, p. 385.	M. 54	—	—	" "	Spindle-celled sarcoma.	Cotterill.	+	...	—	...	Nothing seen or felt; died in 3 months; no pressure symptoms; tumor subcortical.
38	Ibid.	M. 35	—	—	" "	Sarcoma.	"	+	+	—	...	

No.	By whom and where reported.	Sex and age.	Choked disk.	Headache.	Position.	Variety.	Operator.	Recovery.	Cure.	Improvement.	Deaths.	Remarks.
39	Hoche. Deut. Zeitschr. f. Nervenheilk, 1900, p. 149.	F. 54	—	?	R. motor area.	Spindle-celled sarcoma.	B. Lange.	...	...	...	+ 12 days.	Some tumor tissue left.
40	A. Delobel. Gaz. hebd. de Méd. et de Chir., 1900, p. 682.	M. 32	—	—	Median.	Fibrosarcoma.	Verstraeta.	...	...	...	+ 2 days.	
41	Apert & Gandy. Archiv. gén. de Méd , 1900, n.s., iii. 581.	M. 45	—	+	R. motor area.	Fibroma.	Marion.	...	...	...	+	Died next night after temporary improvement.
42	Van B. Knott. Journ. Amer. Med. Assoc., 1900, i. 978.	M. 14	—	+	R. motor area (ant.).	Cyst.	Knott.	+	...	+ great.	...	Thin walls of cyst removed
43	Durante. Brit. Med. Journ., 1900, ii. 1462.	M. 20	+	+	R. frontal area	?	Durante.	+	...	+ great.	...	Recurrence in 8 mos., operation; recurred again in 8 months, and death.
44	Mills, Spiller and Keen. Journ. Nerv. and Ment. Dis., May, 1900.	M. 57	—	+ 1. side.	L. parietal lobe.	Endothelioma.	Keen.	+	+	...	...	Cyst opened in removing tumor.
45	F. R. Sherwood. Chicago Clinic, 1900, xiii. 390.	F. 43	+	+	R. motor area, upper third.	Fibroma from dura.	Sherwood.	+	...	+	+ 2 wks	Temporary improvement.
46	Steffenson. Med. News, Feb. 3, 1900.	M. 32	+	+	L. parietal region.	?	L. D. Rogers.	...	...	...	+ 2 hrs.	Death due to hemorrhage and shock.
47	Hale White. Guy's Hosp. Reports, 1901, lv.	F. 18	+	+	L. nucleus caudatus.	Spindle-celled sarcoma.	White.	+	...	+	...	Temporary improvement after the third and fourth operations; patient finally died.
48	Krönlein. Centralbl. f. Chir., 1901, Beilage, p. 46.	M. 61	—	+	R. motor area.	Spindle-celled sarcoma.	Krönlein.	+	...	...	...	Tumor not found; probably small at operation; died in 1¼ years; autopsy.
49	Heidenhain. Ibid., p. 42.	M. 52	+ left.	+	R. motor and par. area.	Cystic sarcoma	Heidenhain.	+	+	...	...	Tumor subcortical.
50	Ibid., p. 44.	M. 19	+	+	R. temp. lobe.	Melanotic carcinoma.	"	+	...	...	...	Died in 3 months; diagnosis by Edinger. Hearing and musical sense in left ear normal after removal of entire temporal lobe.
51	Clarke and Lansdown. Brit. Med. Journ., Apr. 13, 1901.	M. 26	+ left.	+	Post. inf. angle l. par. bone.	Spindle-celled sarcoma.	.....	+	...	+	...	Second operation in a few weeks, and large tumor removed.
52	H. H. Hoppe. Journ. Amer. Med. Assoc., Feb. 2, 1901, p. 302.	M. 32	—	+	R. motor area.	?	Ransohoff.	+	...	+ great.	...	Nearly a cure; report years later.
53	Ibid.	M. 18	+	+	L. occipit. reg.	Glioma.	R. Sattler.	+	+	...	...	Sight largely restored; at work in a mine 3 to 4 years later.

54	Ibid.	M. 10	+	?	R. motor area.	Tubercle.	Ransohoff.	...	...	...	+ 6 hrs.	Tubercle ¼ in. below bottom of incision, found at autopsy.
55	Ibid.	M. ?	+	+	" "	Gliosarcoma.	"	...	...	...	+ same day.	Death from shock; nothing found at operation.
56	Leszynski and Glass. Med. Record, Sept. 28, 1901.	M. 56	+	—	" "	Endothelioma.	Glass.	+	...	+	...	Report 2 years after operation.
57	J. Stewart. Amer. Med., Dec. 21, 1901.	M. 37	+	+	L. motor area, inf. and ant.	Glioma.	J. Bell.	+	+	...	...	Report 9 mos. after operation; cyst around tumor.
58	Dunning. St. Paul Med. Journ., 1901, p. 78.	M. 62	?	?	R. motor area.	Sarcoma.	C. A. Wheaton	+	+	...	...	Patient a physician, practising 4 years later.
59	Mingazzini. Deutsche Zeitsch. f. Nervenheilk., 1901, xix. 1 et seq.	M. 51	—	+	R. insula and corp. striatum.	Spindle-celled sarcoma.	Montenovesi.	...	...	...	+ 2 days.	Tumor found at autopsy, not felt at operation; fracture 3 months old.
60	Ibid.	F. 38	+	+	L. motor reg. ant. part.	Glioma.	Postempsky.	+	...	+	...	Some astereognosis remains in right hand.
61	Ibid.	M. 40	+	+	L. motor and parietal areas.	Fibrosarcoma.	Durante.	+	...	+	...	X-ray examination negative.
62	C. K. Mills. Phil. Med. Journ., April 20, 1901.	M. 65	+ left.	+ l. side.	L. sup. par. convolution.	Gliosarcoma.	Keen.	...	...	...	+ 2 dys.	
63	Ibid.	M. 8	+ double.	+	R. sup. frontal convolution.	Sarcoma.	"	+	+	...	...	Report 3 mos. after operation.
64	Walton and Paul. Journ. Nerv. and Ment. Dis., 1901, p. 191.	F. y'g	—	+	R. motor and parietal area.	Cyst.	Warren.	+	...	+	...	Died in 4 weeks; temporary improvement.
65	Ibid.	F. y'g	+ late.	+	L. motor area and parietal lobe.	?	Beach.	+	...	+	...	Improvement confined to pressure symptoms; operation palliative.
66	Ibid.	F. 27	+ double.	+	R. motor area and parietal lobe.	Old clot.	Warren.	+	...	...	...	Condition about the same 1 month later.
67	McCuskey and Porter. Journ. Amer. Medical Association.	M. 34	+ first right.	+	R. motor area.	Glioma.	Porter.	+	...	+	...	Tumor felt ½ in. below surface by needling.
68	C. K. Mills and G. E. Pfahler. Phila. Med. Journ., Feb. 9, 1902.	F. 52	+ double.	+	L. par. reg. and motor area.	Fibrosarcoma.	W. J. Hearn.	...	...	...	+ 2 hours	X-ray shadow.
69	Mills, Pfahler & Deaver. Phil. Med. Journ., Sept. 27, 1902.	F. 21	+	+	R. motor area.	Spindle-celled sarcoma.	J. B. Deaver.	...	...	...	+ 3–4 hours	Two stages because of hemorrhage; carotids clamped by Crile's method; X-ray shadow.
70	Ransohoff. Journ. Amer. Med. Assoc., Oct. 11, 1902.	M. 30	—	—	L. motor area.	Solitary tubercle.	Ransohoff.	+	...	+ marked.	...	Report 3½ months later; pulm. tuberc. 5 years ago; operation in two stages; nothing felt till sitting up.
71	Durante. Brit. Med. Journ., 1902, ii. 1822.	F. 35	+	?	L. frontal lobe.	Fibrosarcoma.	Durante.	+	+	...	...	Symptomatic cure; recurrence; second operation 11 years later; same as next case.

No.	By whom and where reported.	Sex and age.	Choked disk.	Headache.	Position.	Variety.	Operator.	Recovery.	Cure.	Improvement.	Deaths.	Remarks.
72	Durante. Brit. Med. Journ., 1902, ii. 1822.	F. 46	?	?	L. frontal lobe.	Fibrosarcoma.	Durante.	+	+	...	...	Symptomatic cure; report 6½ years later; no recurrence.
73	Ibid.	M. 39	+ left.	+	" "	Gumma (subcortical).	"	+	+	...	...	Report 6 years later.
74	F. X. Dercum. Journ. Nerv. and Ment. Dis., 1902, p. 347.	M. 23	+ double.	+	L. motor area and 2d front. convolution	Spindle-celled sarcoma.	Keen.	?	...	...	...	Result not given; hemorrhage severe.
75	W. W. Keen. Ibid.	F. 43	+	+	L. front. lobe.	Spindle-celled sarcoma.	"	...	...	...	+ 4 hrs.	Death from shock; hemorrhage free.
76	C. K. Mills. Phil. Med. Journ., Nov. 29, 1902.	M. 27	+	+	L. motor area.	Gumma.	W. J. Hearn.	+	...	+ great.	...	Report 4 weeks after operation; X-ray shadow.
77	E. v. Bergmann. Archiv f. klin. Chir., 1902, lxv. Heft 4.	M. 34	+ right.	+	R. front. reg.	Angiosarcoma	v. Bergmann.	+	...	+ great.	...	
78	Ibid.	M. 4½	+ double.	...	L. motor area.	?	"	...	...	...	+	Death due to shock.
79	Ibid.	M. 44	—	+ l. side.	" "	Cavernous angioma.	"	...	...	...	+	Death from hemorrhage.
80	Ibid.	F. 46	+ right.	+	" "	Round-celled sarcoma.	"	+	...	...	+ 15th day.	Died of purulent meningitis; tumor only felt when patient sat up.
81	C. Thiem. Centralbl. f. Chir., 1902, Beilage, p. 56.	M. 38	+ right.	+	L. occip. lobe.	Cystic tumor.	Thiem.	+	+	...	...	Right hemianopsia present.
82	W. Elder and A. Miles. Lancet, Feb. 8, 1902.	M. 47	+	+	L. prefront. reg.	Gumma.	Niles.	+	... great.	+	...	Report 4 mos. after operation.
83	Gussenbauer. Wiener klin. Woch., 1902, p. 1434.	M. 11	+ right.	+	R. motor area.	Gliosarcoma.	Gussenbauer.	+	...	+	...	Died in 4 months or more; operation palliative; nothing seen or felt.
84	Ibid.	M. 42	—	+	L. motor area.	Large round-celled sarcoma.	"	+	...	+	...	Recurrence; death 2 years after operation.
85	Ibid.	M. 22	+	+	?	?	"	+	...	...	...	Result negative; nothing seen or felt.
86	Ibid.	M. 31	+ right.	+	L. motor area.	Sclerosis of cortex.	"	+	...	...	...	Worse rather than better.
87	Ibid.	F. 12	+ right.	+	R. motor area.	Gliosarcoma.	"	+	...	+	...	Well 2 years later; died 3 years and 1 month after operation; lateral ventricle probably opened.
88	Ibid.	M. 38	—	+	" "	Gumma.	Funke.	+	...	+	...	Last seen 2½ months after operation.
89	Ibid.	F. 24	—	+	" "	?	Föderl.	+	...	+	...	Symptoms persist 1 year after operation; nothing seen or felt at operation.

90	Ibid.	M. 53	—	+	L. motor area, post. part.	Necrotic tissue.	Gussenbauer.	+	...	+	...	Report 2 weeks after operation; local tenderness on percussion present.
91	Ibid.	F. 13	+	+ l. side.	L. motor area.	Cyst.	"	+	...	+ great.	...	Last report 1 month after operation; left parietal resonance tympanitic.
92	Ibid.	F. 38	+ right.	+	R. motor and sup. front. area.	Gliosarcoma.	"	+	...	+	...	Improvement lasted 7 mos.; death 7 mos. after operation.
93	Ibid.	M. 43	+	+	R. motor area?	?	"	+	...	+	...	Improvement temporary; death 6 months after first operation; nothing found at first or second operations.
94	Ibid.	F. 21	—	+	L. front. reg.	Round-celled sarcoma.	"	...	...	...	+ 5 hrs.	Painless frontal tumor.
95	Starr & McCosh. Presb. Hosp. Reports, 1902, p. 1.	F. 45	+	+	R. motor area.	Small round-celled sarcoma.	McCosh.	+	...	+	...	Report 1 year after operation; astereognosis remains in left hand.
96	Kiliani. Ann. of Surg., April, 1903, p. 610.	M. 32	+	+	L. motor area.	Gliosarcoma.	Kiliani.	+	...	+	...	Died 4½ mos. after operat'n from infection of persisting sinus; X-ray shadow.
97	Woolsey. Ibid., Feb., 1903, p. 274.	F. 46	—	+	L. motor and par. area.	Sclerosis of cortex.	Woolsey.	+	...	+	...	Improvement continues 1½ years after operation.
98	Ibid., p. 276.	M. 19	+ double	+	R. motor area.	Fibroma and cyst.	"	+	+	...	...	Astereognosis present for a time; patient well 8 mos. after operation; cyst ruptured spontaneously.
99	Ibid. Not reported; see above.	F. 29	+ right.	+	R. occip. lobe.	Glioma.	"	+	...	+	...	Improvement marked for a time; died 8½ mos. after operation; left hemianopsia present.
100	Ibid. Not reported; see above.	F. 18	?	?	R. motor area.	Cyst.	"	...	...	...	+ 36 hours	Collapse after 4 hours; very high temp.; no apparent infection; cyst extended back beneath motor area.
101	Ibid.	M. 39	?	+	R. front. reg.	"	"	+	...	+	...	Cyst extended back toward and beneath motor area, opened and drained; celluloid plate over opening.

This series of 101 cases includes five cases of tumor localized in the parietal region and found and removed by operation, besides one imperfectly localized from an insufficiency of focal symptoms. Four of these five cases were localized and reported by Mills, of Philadelphia. All of the five cases presented symptoms of sensory disturbance, and were localized by these symptoms. In four of them these symptoms included astereognosis, which was also present in the case of some tumors in the motor area where the region behind it was invaded. With reference to astereognosis, Walton[4] concludes that "it seems a safe working plan in operable cases with no other localizing symptom than astereognosis to select for the centre of the area to be exposed a point in the ascending parietal convolution at a height corresponding to the motor representation of the extremity involved." In four of the five parietal tumors there were also motor symptoms, usually of moderate development and late appearance, and due to the forward extension of the tumor or its pressure in the course of its growth. Three of the cases also presented ataxia.

Three of the 101 cases were diagnosed and found in the occipital lobe. In all three there was homonymous hemianopsia which, says Bruns,[3] alone or associated with appearances of optic irritation or hallucination or soul-blindness, is characteristic of tumor of the occipital lobe. Schuster[1] says that hallucinations and delirium are particularly frequent in occipital lobe tumors. In one case there was also an external tumor to assist in the localization. Among the 273 cases of operated brain tumor collected in v. Bergmann's work,[5] only three of the occipital lobe are given. As the three cases out of the series of 101 include one of the writer's cases which has not been elsewhere reported, a résumé of it is given:

H. S., female, aged twenty-nine years. Family and previous history negative. No specific disease. One and a half years ago intense right occipital headache, nausea, and vomiting. Later on staggering, but to no particular side. Eyes—left: optic neuritis; right: atrophic disk, total blindness. Left hemianopsia. Patient dull and stupid. Semicoma alternating with delirium. Has had drawing up and twitching of left leg. Pulse rapid, weak, and hardly perceptible. Diagnosis by Dr. E. D. Fisher: Tumor of right occipital lobe.

Operation, June 9, 1897. Right occipital lobe exposed by trephine and rongeur, and explored to falx and tentorium. Brain surface appeared abnormal, darker and yellower than normal, and a section was removed for examination. No limited tumor. Two and a half drachms of clear, straw-colored fluid removed by syringe from right lateral ventricle. Dura and scalp sutured. Primary union. June 25th, great improvement; no headaches, stupor, or delirium; patient quiet and rational. Discharged improved June 29th. Microscopic examination of specimen shows it to be a diffuse glioma. She died in September, 1897. The operation was merely palliative.

Enough has been said to show that tumors in the prefrontal, parietal, and occipital regions are localizable and operable, and many of the characteristic symptoms of tumors of these three regions which made this localization possible have been given. Moreover, the results of operation on tumors in these regions have been quite as good as on those of the motor area. The number also of operations on tumors in regions other than the motor area has largely increased in the last five years, and we may justly claim that the indications for operation on cerebral tumors should be extended beyond those of the motor region.

Although in cases of brain tumor the diagnosis should be made or confirmed by a skilful neurologist, the surgeon should not be dependent on this diagnosis alone and operate in a mechanical way like a mere mechanic. To obtain the best result and to intelligently meet the demands of the situation in an operation for brain tumor, the surgeon should have a good knowledge of the methods of diagnosis and localization as well as of craniocerebral topography. We may go a step farther and assert with Durante,[6] in presenting a number of operated cases of tumor of the prefrontal region as a contribution to the function and localization of this part of the brain, that the surgeon in operating on cerebral lesions may contribute much to the physiology of the brain as well as to the diagnosis of its lesions. He likens the surgeon to a physiologist performing an experiment *in vivo*.

In arriving at the *diagnosis* we must consider (1) the general or pressure symptoms, and (2) the focal or localizing symptoms. Of the pressure symptoms, headache, choked disk, vomiting, and vertigo are the most important. Persistent headache is the most constant. In the above 101 cases its absence was mentioned in only eleven cases, or 10.8 per cent. It is of but little value in localizing the tumor, for it was confined to the same side in only ten cases, or 9.9 per cent. It is noteworthy that in tumors of the frontal lobe the headache, if localized, may be frontal or occipital, or both, as the pressure seems to be exerted in both a forward and a backward direction.

According to Wilder,[7] choked disk is present in 80 per cent. of cerebral tumors (90 per cent. of cerebellar tumors), and it is said that 90 per cent. of the cases of choked disk are due to brain tumor. In the present series, among the ninety-four cases where it was mentioned, it was present in only 69.2 per cent.; but among the twenty-nine cases where its absence was noted nothing was found in three cases, cysts in five cases, sclerotic or necrotic tissue in two cases, tubercle in two cases, a gumma and a very small tumor each in one case. Deducting these fourteen cases, choked disk was present in 84.1 per cent. of the remaining cases. Wilder also says that it is of little value as a localizing sign, and that it does not furnish any information as to the nature or size of the tumor; but Gunn[8] states that optic neuritis on one side or

markedly prominent on one side points to a tumor of the cerebrum on that side. In sixteen cases (17 per cent.) of the ninety-four it appeared, first, most markedly or only on the same side as the tumor, and in six cases on the opposite side.

In general, also, it is probably true that it is more regularly present and more often pronounced and double in a large or rapidly growing tumor, and more often absent in a cystic tumor. With tumors of the motor cortex double choked disk appears late, and is frequently absent —*i. e.*, in 33 per cent. of cases according to Wilder and in 38 per cent. of my series of 101 cases. Hence in tumors choked disk of the motor area, and especially double choked disk, indicates a large or rapidly growing tumor.

In an analysis of seventy-four cases of cerebral tumor Singer "found the absence of optic neuritis rare in cases under forty years of age, and increasingly common after that." Among the fifty cases under forty years in which choked disk is mentioned, it was absent in thirteen (or 26 per cent.) against 44 per cent. in cases over forty years. Among the thirteen cases just mentioned are nine which we deducted in taking the percentage of choked disk, making choked disk absent in only 8 per cent. of cases under forty years of age.

In the present series of cases vomiting and vertigo were present in a relatively small proportion of cases, 33.3 per cent. and 22.2 per cent., respectively. Still other pressure symptoms occur, such as slow pulse, deep respirations, psychic unrest, or general convulsions; but the decisive pressure symptom is choked disk.

Without going into a discussion of the mechanism of the pressure symptoms and the various theories which seek to explain them, we may say that some of the cases operated upon show the importance of the cerebrospinal fluid as a factor in the pressure symptoms, and thus support v. Bergmann's theory that the increased tension of this fluid compresses the capillaries and causes anæmia, and thus irritation and paralysis of the nerve centres.

While the pressure symptoms, combined with the course of the disease and exclusion, may enable us to diagnose a brain tumor from other brain lesions, they do not enable us to localize it so that we are justified in attempting its removal. An exact localization, says Oppenheim, is necessary for surgical treatment; and "only the relative certainty of the diagnosis gives us the right to do a dangerous operation" is the statement of v. Bergmann. The focal or localizing symptoms, due to the destruction of or the local pressure on some particular part of the brain whose function is known, vary with the position of the new-growth and hence lead to its localization.

There are two other means of localization of brain tumors that may prove of much assistance—percussion or pressure and the X-ray. In

the series of 101 cases collected local tenderness on percussion or pressure over the tumor was noted in twenty-one cases. Two of these were subcortical, including one tubercle, the remaining nineteen cortical or surface growths, including two cysts, three gummata, one case of necrotic tissue, and three cases of painful tumors, appearing on the surface. If percussion or pressure show tenderness locally the tumor is probably superficial.[5] Macewen has called attention to changes in resonance on percussion over cerebral tumors—*i. e.*, tympanites, increased dulness, and cracked-pot sound—which are of service in localization when circumscribed, and in general diagnosis when more diffuse. In two cases on the list increased dulness was noted, and in one case (No. 51) it was the only marked localizing sign. In two cases there was tympanitic resonance, and in one of these cases (No. 75) also this symptom and local tenderness were the principal localizing signs. In cases of difficult diagnosis the local tenderness and percussion note may be even more important than the cerebral symptoms.[5] Carson[9] reports a case to show that the cranial cracked-pot sound may be a valuable sign of cerebral tumor, and claims that it is due to a separation by pressure from within of the sutures which had previously come together. In one case (No 63), in a child of eight years, there was a cracked-pot sound on both sides. It is to be remembered that changes of the cranial percussion note are present in other conditions than tumors, especially traumatic lesions associated with blood clot. (See also Paoli and Mori, *Il Policlinico*, February 15, 1898.) In six cases of the series there was an external swelling, three of which were tender to pressure. The X-ray has only lately been tried in cases of suspected brain tumor. In one case of the series (No. 61), a glioma of the motor area, it was negative; while in four others (Nos. 68, 69, 76, and 96), including three sarcomata and a gumma, it was positive. These and a case of glioma of the cerebellum reported by Church, of Chicago, include all the reported cases that I know of where the X-ray was positive. In two of these cases the bones of the vault were noted as being very thin. Obici and Bollici[10] demonstrated post-mortem by means of the X-ray a sarcoma of the brain in a boy, proved it by dissection, and experimented on the cadaver. The great importance of attention to special details in this work is emphasized.

For the purposes of operative treatment it would be very desirable to have a still more exact diagnosis, to know whether the growth is cortical or subcortical, and what its size and nature are. It was pointed out some time ago by Seguin and Mills that paresis with predominance of tonic spasm, such as frequent attacks of Jacksonian epilepsy, indicate a cortical lesion, though this symptom is present in a few subcortical tumors. If percussion be very sensitive locally the tumor is probably superficial. In large tumors the symptoms due to pressure are usually

very marked, and the focal symptoms indicate a wide extent of involvement or pressure. Tumors of the motor cortex where double optic neuritis is marked are probably of large size.

We are still less able to diagnose the nature of the tumor. Pressure symptoms, including choked disk, are probably less common or less marked with a cyst than with a solid tumor of equal size, though it is difficult to diagnose a cyst from a small, solid tumor. Rapidly growing tumors, as indicated by the course of the symptoms, should indicate malignant growths, glioma, sarcoma, etc.; but many of the latter grow slowly, as indicated by the duration of the symptoms in such cases. This is especially true of the fibrosarcomata and spindle-celled sarcomata, fourteen cases of which averaged nearly three years, while the small round-celled variety shows a much shorter duration. We know, too, that the so-called malignant tumors are by far the most common. Thus, in this series of cases, among the eighty-eight cases in which the variety of the tumor was mentioned, forty-four (50 per cent.) were sarcomata (including gliosarcoma), eleven (12.5 per cent.) were gliomata, ten cysts, five fibromata, five gummata, three tubercles, two angiomata, two endotheliomata, two cortical scleroses, and four single examples of other forms. There were also six cases in which nothing was found and six in which the variety was not mentioned.

At times we may diagnose with some certainty a gumma or a tubercle from the previous history or the present condition. We can rarely, if ever, tell whether a tumor is encapsulated or not, though Singer[11] says that out of seventy-four cases of autopsied cerebral tumors all of the nine which had had no optic neuritis were over forty years of age and had infiltrating malignant growths.

The importance of the accurate localization of cerebral tumors is shown in Van Hippel's statistics, given by v. Bergmann,[5] in which out of 116 cases accurately localized the tumor was removed in all, 60 per cent. were improved or cured, and 7 per cent. were not improved or died of the operation. On the contrary, in 157 cases where the localization was defective and the operation was more or less exploratory, 47.7 per cent. died as the result of operation. Out of 111 cases collected by Knapp[12] where the tumor was not found, fifty-eight (52 per cent.) died, and in about 21 per cent. of all operated cases there was a failure to remove the tumor owing to errors in diagnosis.

The *indications* for operative treatment are clear. A radical operation is indicated in cases where the tumor can be satisfactorily located in a region accessible to surgical operation and when there is no evidence of malignant disease elsewhere, of a very large cerebral growth, or of multiple growths. V. Bergmann is opposed to operation on supposed gummata, Horsley in favor of it, and the weight of evidence is in favor of the latter view. The mortality and results are more favorable with

gummata than with any other form of new-growth. Moreover, other forms of tumor may occur in those giving a syphilitic history, as occurred in at least one of the appended series of cases, and a gumma may occur when no history of syphilis is obtainable; so that we cannot be sure of the nature of the growth until we have exposed or, perhaps, even examined it. Although antisyphilitic treatment may temporarily improve the symptoms due to a gumma, and even those due to other forms of tumor, it probably rarely, if ever, causes the entire absorption of the gumma, so that an operation is the only sure radical cure.

Solitary tubercles have also given good results, Horsley's and other cases having remained well five to seven years.

Opinion is divided as to palliative operations, but personally I think they are strongly indicated where the tumor is not to be localized or is inaccessible, in order to relieve the symptoms most complained of—headache, loss of vision, etc.—when these are pronounced. Such operations are comparatively safe. Knapp[12] gives 14 per cent. of mortality in sixty-eight cases, and I think this figure is too high for the present results. The temptation to make such an operation a thorough exploratory one should be resisted, for the weight of opinion is against exploratory operations.

The *prognosis* is hard to give in advance, so much depends upon the conditions found. It should never be lost sight of, that all cerebral tumors, even the most benign, are necessarily fatal if nothing is done for them. The mortality, according to the statistics of Chipault and of Starr, is about 56 per cent.; the tables of Knapp make it 43 per cent. before 1891, 33.4 per cent. from 1891 to 1898. In 1899 v. Bergmann found that 25 per cent. of cases died as the direct result of the operation. The improvements in localization and operative technique have reduced the mortality of cases operated on in the last five years. In the series of cases I have collected, twelve cases (11.8 per cent.) died within twenty-four hours and twenty-six (25.7 per cent.) within three weeks. If we select the eighty-eight cases where an exact localization was made, the mortality was somewhat less—22.7 per cent. as against 46 per cent. among those not exactly localized. In the table are twelve cases of Gussenbauer's, with only one death, and that due to pneumonia. As to the more remote prognosis, six died between three weeks and three months, nine between three months and one year, and three between one and two years. As almost all of these died from the effect of the tumor, the mortality within two years is 43.5 per cent. This probably does not represent the actual mortality within this period, for a large number are reported within a comparatively short time after the operation—in one case only two weeks.

In spite of the high mortality we must admit that the immediate and remote mortality is no greater than follows radical operation for malig-

nant growths in some other situations. When we consider the otherwise hopeless condition of these cases, the difficulties of exact diagnosis, the inaccessibility of the tumors, and the marked relief of symptoms in almost all cases not dying at once, we may take courage and feel some degree of satisfaction. When we look at the other side of the question —the length of time during which some cases remain free of recurrence —we may feel still more encouraged. Cases of sarcoma are reported four years, four years and one month, five and one-half years, and eleven years after operation. The last case—one of Durante's—then recurred, was again operated and was well six and one-half years later. A case of fibroma was reported well eight years, cases of gummata two and two and one-half years, a case of glioma three and one-half years, and one case, in which the variety of tumor was not given, nine years after the operation. Seven cases of sarcomata are reported to have recurred at periods ranging from three months to eleven years, and averaging two years and four months or, exclusive of the latter case, nine and one-third months.

Gussenbauer[13] says that in gliosarcomata the prognosis can be made only with great reserve even when removal is apparently within normal tissues. In one of his cases recurrence was first evident after three years. McCosh removed a brain tumor, pronounced fibroma by the pathologist, which recurred as a sarcoma in a few months. Naturally the remote prognosis of malignant tumors anywhere is not good at best, especially when not encapsulated; so that the above results are far from discouraging. At least we do not have to fear glandular metastasis in the malignant tumors we meet with in the brain. In reference to recurrence, v. Bergmann says that among the tumors which grow in the cortex, and can therefore be reached by the knife, those are most frequent which promise favorable results from an operation, viz., tough fibromata and sarcomata which are well encapsulated, have their seat of predilection in the gray matter of the cortex, and, when once removed, do not seem to recur.

The prognosis of cysts should not be given without reserve. My first case, operated in 1893, is an example of this. K. R., female, aged eighteen years; fracture of right temporofrontal region at two and one-half years, followed by three operations. At seven years Jacksonian epilepsy on left side, with aura in left hand extending to left foot; tremor of left extremities. Operation: right motor area exposed, and appeared normal; old scar and gap in bone exposed; cyst opened leading back to beneath motor area; drainage; four hours later collapse; temperature 104° F.; stimulation and reaction; unconsciousness; temperature rose to 108° F.; death in thirty-six hours; no autopsy; no apparent infection. Without particular care there is always the danger of infection in a cyst as long as drainage is employed. As to the remote

prognosis of cysts, v. Bergmann says that traumatic cysts are not common and of small size, and that brain cysts more often occur in sarcomata of the brain from the softening and breaking down of nearly the entire tumor. When the fluid of a brain cyst is rich in albumin, and the cerebrospinal fluid from a lumbar puncture is poor in albumin, the cyst is always one derived from a sarcoma. In a case of Vallor the sarcomatous nature of the cyst was first known after three years.

In the evolution of the *technique* the *operation* of craniectomy for the exposure and removal of cerebral tumors has undergone many changes and great improvements, with a resulting lessening of the mortality. It is significant that infection was the cause of death in but two cases on the list. Trephining and enlarging the opening by the rongeur was too slow, and if a sufficient exposure were obtainable an unpleasantly large opening was left in the skull. The Wagner osteoplastic flap was a great advance, and revolutionized cerebral surgery, for a large area is rapidly exposed for examination, plenty of space is afforded for operation, and by replacing the flap the objection of leaving a large, uncovered area of brain is obviated. But here, too, the chisel and mallet were somewhat slow and theoretically liable to cause concussion, though I have not found it so in practice. Mills[14] says it is of the utmost importance that some speedier method of opening the skull, and some method accompanied by less cranial concussion, should be employed. In my last two cases I have employed with satisfaction Doyen's electric circular saw. A small opening is rapidly made with a burr at each angle of the quadrilateral flap, the thickness of the skull is measured at these openings, and a collar of such a size adjusted on the saw that the latter will not quite cut through the inner table. The latter is broken by the blow of a chisel with a probe-pointed lower angle, and the flap is raised up, breaking the base as a hinge for the flap. This fracture may be facilitated by sawing partly through from beneath with a Gigli saw, and the latter may be used for the entire sawing required, but it takes considerably longer. If one uses the Gigli saw slowly no protection of the dura is necessary. I have had no experience with the Stellwagon trephine, but it does not seem to have fulfilled its promise.

Hemorrhage is an important factor in these operations, and I am convinced that it is the chief cause of shock in the surgery of cerebral tumors. In two or more cases in the series death was directly attributed to it, and in at least four cases the operation was done in two stages on account of hemorrhage.

It is naturally free from the scalp, and sometimes unusually so. I have often controlled it by elastic tubing drawn tightly around the head above the eyebrows and ears, or, when this fails, by temporary overlapping interrupted silk sutures below the base of the flap, and

above it if necessary. Continued oozing from the cut surface of the bone may be controlled by pressure with or without the use of Horsley's powdered wax, pressed into the diploë. If we minimize the hemorrhage in the first part of the operation I think it will seldom be necessary to follow Horsley's advice to operate in two stages, going as far in the first operation as raising the bone flap. After losing a case from hemorrhage, v. Bergmann advises this plan when the first stage of the operation causes symptoms of collapse. This was practised in at least four cases in the series of 101 cases, and in one case (No. 69) at the second operation Crile's plan of temporarily clamping the carotids was employed.

The flap of dura, cut about one-quarter of an inch from the bony margin, may be turned back in the same or, according to Keen, in the opposite direction to the bone flap. The stage of approach to the cortex is now finished, and if the tumor is in or on the cortex its removal is usually a simple matter. After incising the pia about them, most tumors—unless disseminated or not encapsulated—are best shelled out with the finger. If nothing is seen on the cortex, the tumor, if present, must be subcortical, and to find it we first palpate the surface exposed. If we cannot feel it, v. Bergmann advises raising the patient to a sitting posture, whereupon the tumor may become visible or palpable, the area exposed sinking in somewhat from the atmospheric pressure in connection with the lessened blood pressure. This plan was successfully used in one case (No. 70) by Ransohoff. If this fails, electrical stimulation may be and has been used to exactly locate the explosion centre of the Jacksonian attacks. Singularly enough this not infrequently gives no muscular contractions, a fact explained by some by supposing that the deep anæsthesia inhibited them; but the same result has been obtained when the patient was allowed to partly come out of the anæsthesia.

If this means fails, then, locating the centre of the area involved, as indicated by the diagnosis, as accurately as possible from the landmarks of the exposed area, we may make a small anteroposterior incision through the cortex and explore with a probe, grooved director, aspirating needle, or the little finger. The first three may be carefully introduced in various directions. Unless we have a positive result with the X-ray, we would not be justified in going any farther. The above exploration is proper and indicated in cases confidently localized; contraindicated in those that are not. An example of a spontaneous disclosure of a tumor and cyst was presented by my last case operated upon (No. 98), where on laying back the dural flap the brain protruded very prominently, its cortex ruptured and opened a subcortical cyst, which forcibly evacuated itself on account of the increased pressure. On enlarging the opening I enucleated a tumor, a fibroma, by means of the

finger, from the mesial wall of the cyst. (See *Annals of Surgery*, February, 1903, p. 276.)

Bleeding from the cavity left by the tumor should be controlled, as far as possible, by ligature or gentle packing. I believe in always leaving a drain, at least of folded rubber tissue, through the sutured dura to give outlet to the oozing; otherwise the bleeding, which may start afresh, may work its way into the surrounding brain tissue, like a cerebral hemorrhage, or between the dura and brain, and thus add to the area of brain substance destroyed or cause cerebral compression. The drain may be removed in forty-eight hours.

I have never had any trouble from hernia cerebri, though it is still a not uncommon complication, due, in many cases at least, to lack of drainage or to infection. Suture of the pericranium and scalp, allowing for free drainage, completes the operation.

In palliative operations, and where the tumor cannot be found, the bone should be removed from the flap to relieve the increased intracranial pressure and the symptoms due to it, introducing rubber tissue or, better still, a thin plate of celluloid, to prevent union of the scalp and dura. In a considerable number of flap operations for various purposes I have had no failure of union of the bone flap.

The results vary from a nearly complete cure to the relief of the distressing pressure symptoms, and in a few cases no improvement whatever has been noted (6 out of 101).

Absolute cure or *restitutio in integrum* is rarely, if ever, to be expected on account of the necessary damage to the brain substance by the tumor and the operation of enucleating it; still, in 16 out of 101 cases (including my last case) the symptomatic result was so good as to be considered a cure, and in forty-one cases the result has been improvement, often so marked as to be nearly a cure.

In spite, then, of the small percentage of operable cases, the difficulties of diagnosis, the uncertainty of prognosis, the fairly high mortality, the liability to recurrence, and the difficulties of the operation, and in view of the results obtained and the fact that even benign cerebral tumors are necessarily fatal, I think that the radical operation is justifiable and indicated in selected cases, and the palliative operation in another group of cases of cerebral tumors.

I would like to emphasize the following conclusions:

1. The sphere of operation for cerebral tumors may be and has been extended to those parts of the cortex where tumors are accessible and localizable—*i. e.*, to the prefrontal, parietal, and occipital regions, in addition to the motor area.

2. The prognosis, both immediate and remote, is as good as or even better than in operations for malignant growths in some other locations.

3. This prognosis has improved with the improvements in localization

and operative technique, and with the limitation of the radical operation to cases accurately localized.

4. The palliative operation is strongly indicated to relieve symptoms where localization cannot be accurately made or the tumor cannot be removed. The exploratory operation is contraindicated.

5. Practically all circumscribed growths of moderate size are suitable for operation.

6. The osteoplastic method should be employed and the most rapid and perfect technique adopted which the circumstances allow.

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MULTIPLE SCLEROSIS WITH DEMENTIA: A CONTRIBUTION TO THE COMBINATION FORM OF MULTIPLE SCLEROSIS AND DEMENTIA PARALYTICA.*

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INTRODUCTION. Disseminated sclerosis of the central nervous system is generally accompanied by slight mental changes. In the larger number of cases the psychical alterations are insignificant, of mild character, and playing a minor rôle in the list of symptoms. They may be summed up briefly as follows: mental dulness and apathy; mild states of exaltation or depression and emotional instability; undue mental complacency and contentment.

With the progression of the affection and the increase of the general symptoms the mental impairment suffers still more, so that in the later stages a partial dementia is not uncommon.

Another group of cases with the somatic symptoms of disseminated sclerosis is characterized by a preponderance of the mental symptoms,

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these appearing early in the course of the disease, of unusual severity, and terminating in complete dementia.

This group is represented pathologically by two subdivisions:

1. An extreme development of the sclerotic process in the gray and white matter of the brain (cerebral type of disseminated sclerosis).

2. A mixed or combined form. Dementia paralytica and multiple sclerosis occurring in combination.

Both are very rare. The following case represents the combination form of the two diseases:

SUMMARY OF CASE.* A woman, aged fifty-three years, presenting the symptoms of multiple sclerosis followed by dementia: spastico-ataxic gait; nystagmus; ataxic and intention tremor of arms; impulsive laughter; syllabic speech; double optic neuritis; progressive mental enfeeblement, terminating in dementia; duration, eight years.

Autopsy. Thickening of the calvarium; opaque and thickened meninges; marked atrophy of the frontal lobes; granular ependymitis; dilatation of the ventricles; disseminated plaques of sclerosis in the brain, cerebellum, pons, medulla, and cord.

Histological characteristics of general paralysis and disseminated sclerosis.

Clinical Notes. R. M., aged fifty-three years, was admitted to the Montefiore Home for Chronic Invalids October 2, 1896. She was the mother of seven children, two dying in infancy of negative causes. No miscarriages; no history of a syphilitic affection was obtainable. Her symptoms date back four years, and had followed an exposure to cold, beginning with uncertainty and weakness in the legs, which had grown progressively weaker.

Her memory is very defective. This with considerable mental enfeeblement render an accurate previous history impossible.

On admission patient was awkward in all her movements; gait spastico-ataxic; pronounced static ataxia both with open and closed eyes; ataxia and weakness of both upper extremities; right hemiparesis; speech stammering and syllabic; impulsive laughter; facial expression one of stupid hilarity; sight subjectively not impaired; examination of the internal organs negative.

Ophthalmological Examination. (Dr. Oppenheimer.) Double optic neuritis passing into atrophy.

Note, June 14, 1897. (Examination by Dr. Joseph Fraenkel.) Patient is good-natured, complacent, and inclined to hilarity; complains of occipital tenderness and pains in the upper and lower extremities. Subjectively vision is not impaired. General paræsthesia (numbness and pricking), especially in the extremities. Pupils are small; all reactions present. The lateral excursions of the eyeballs are somewhat limited. Distinct lateral nystagmus.

The lower extremities are paretic, and passive movements encounter resistance. Ataxia and awkwardness of both upper extremities, especially the right.

No objective sensory disturbances.

* Presentation of Clinical History and Specimens at a meeting of the New York Neurological Society, February 4, 1902.

The jaw-jerk and the tendon-jerks of the upper extremities are wanting. The knee-jerks are lively and equal on the two sides. Ankle-jerks feeble on both sides and easily exhaustible.

Epigastric and abdominal reflexes absent; no involvement of the sphincters.

Note, June 25, 1899 (Dr. Fraenkel). Patient good-humored, silly, hilarious. Memory very poor. Says she has never been ill in her life. Extreme mental deterioration. Speech is stammering, with now and then a trace of syllabification. She can neither walk nor stand, and a change of position in bed is effected with great difficulty. Lower limbs are held in a state of flexion. Occasional involuntary atactiform movements of the arms and head.

The eyeballs are constantly dancing, and all movements except downward are accompanied by nystagmus. Pupils of equal size, well shaped, and the reactions to light and accommodation are present. Examination of the vision is unsatisfactory, but no serious defect is present. Sense of smell and hearing are apparently preserved. Motor cranial nerves are normal.

The arms are weak, especially the right. No atrophy. Marked inco-ordination on both sides. On lifting a glass of water to the lips a typical intention tremor is elicited. Tendon reflexes not elicitable. No objective signs obtained.

The lower extremities are paretic and held in semiflexion. Of good volume. No resistance to passive movements; on the contrary, a slight degree of hypotonia exists. Slight hyperæsthesia; otherwise sensation normal. The right knee-jerk is lively; the left absent. The right ankle-jerk is present; the left absent. Plantar reflex is present on the right, absent on the left.

The muscles of the trunk are normal. Epigastric reflex absent. Electrically the muscles of the legs present sluggish faradic response. Reaction to the galvanic current normal. Died December 28, 1900.

Post-mortem Examination. The autopsy was performed December 29, 1900, by Dr. Harlow Brooks. A small tuberculous focus in the left apex. Purulent bronchitis. Interstitial nephritis. On removing the calvarium the anterior portion corresponding to the frontal lobes was found considerably thickened and eburnated, measuring from one-half to three-quarters of an inch. The inner surface of this thickened area is uneven, presenting nodular outgrowths and irregularities. The dura mater is normal. Moderate hydrocephalus *externus ex vacuo*. The leptomeninges are opaque and thickened, especially over the anterior aspect of the brain.

The convolutions of the frontal lobes are narrow and atrophic, the fissures wide and flaring. The whole anterior half of the brain, including the frontal and parietal lobes, appears small and compressed in contrast to the posterior portion. The ventricular cavity is enlarged. Moderate granular ependymitis. The vessels of the circle of Willis are free from arteriosclerotic changes.

After treatment with Müller's fluid the brain and cord were divided into serial segments for the demonstration and localization of plaques of sclerosis. Yellowish plaques of sclerosis sharply demarcated from the normal brain substance were found in the centrum semiovale on both sides in the cerebral cortex and in the cerebellum. These with the exception of a more diffuse sclerosis of the walls of the posterior

horns of the lateral ventricles were small and insignificant. Plaques were also present in the pons and the medulla bordering on the fourth ventricle and dipping down along the raphe. The plaques in the cord were very numerous, chiefly in the cervical and dorsal regions, including both the gray and white matter, with a predilection for the posterior and lateral columns. A few scattered foci were also present in the lumbar cord.

Microscopic Examination. Brain: The cortex is the seat of extensive changes; the cellular elements are tightly packed together and the glia cells are increased. The normal markings of the cortex are effaced. Many of the ganglion cells are sclerosed and atrophied. In many areas

FIG. 1.

Frontal lobe. Showing loss of the cortical fibre-system. Weigert's method.

the leptomeninges are thickened and infiltrated with round cells. The cortical arterioles are thickened, with increase of their nuclei, and the capillaries are increased in number.

The perivascular and pericellular spaces are enlarged, many enormously so, containing pigment, fat-granules, and detritus.

By the Weigert method a considerable loss of the radiating and association fibres of the cortex was demonstrable in the frontal, temporal, and occipital lobes. (Fig. 1.) In these areas the tangential fibres were absent.

In the Rolandic area, however, the cell changes were less intense, the medullary network better preserved, and the tangential fibres were

demonstrable. (Fig. 2.) No excess of pigmentation of the cells was noted, and the corpora amylacea were few in number. The cortical vessels were thickened and increased in number, but no widespread vascular or perivascular inflammatory process was noted.

Cord: The plaques of sclerosis in the brain and cord were composed of a dense network of glia cells and fibrillæ, either matted together in a dense network or arranged in rows and whorls. In these areas when dense the medullated nerve fibres had disappeared. By special stains (Mallory and Van Gieson) many naked axis cylinders were found present.

On the periphery of many of the plaques tongues and prolongations composed of glia cells radiated into the normal cord substance. The vessels in the sclerosed areas were considerably thickened, and the ad-

FIG. 2.

Rolandic area. Cortical network well preserved. Weigert's method.

jacent pia mater was thickened and occasionally infiltrated with round cells. The ganglion cells were of normal configuration and structure. The anterior and posterior roots were normal. Except the moderate round-cell infiltration of the meninges bordering the foci of sclerosis, there were no evidences of an exudative or myelitic process.

By the Weigert-Pal method the sclerosed areas were white and sharply defined, as if cut out with a knife. (Figs. 3 and 4.)

By the Marchi method the sclerotic foci were found free from myelin globules or granule corpuscles.

In portions of the cord not the seat of sclerosis many fibres showed the characteristic reaction, staining intensely black. In other fibres

this degeneration was only partial, a semilunar or concentric ring enclosing a normal axis cylinder. These fibre degenerations were diffuse and nowhere limited to the tract systems.

In the midlumbar region symmetrical patches of sclerosis occupy the tips of both posterior horns, on one side encroaching on the tract of Lissauer and the posterior root zone (anatomical explanation of the absent knee-jerk and Achilles jerk on the left side). The cauda equina was normal. There were no systemic degenerations in the long tracts of the cord.

Optic Nerves and Chiasm: Transverse section of the optic nerves just below the chiasm revealed numerous islets of sclerosis, most numerous in the central portions of the nerve. The nerve sheath is moder-

FIG. 3.

Rolandic area. Sclerotic plaque. Weigert-Pal method.

ately thickened. The islets of sclerosis consist of a much thickened bloodvessel wall, considerably diminishing the calibre of the lumen and a dense perivascular sclerosis. Surrounding and radiating from this as a centre is a fine glia network. In and around these areas the nerve elements are absent or diminished in number (Weigert method).

No round-cell infiltration or other evidences of recent inflammation were discoverable. Numerous amyloid bodies. The centre of the nerve fibre appeared pale in comparison to the deeply stained periphery by the Pal method, but the evidences of nerve atrophy were moderate. The same changes—vascular sclerosis and perivascular gliosis—were noted in the nasal portion of the optic tracts as they merge into the

commissure. No sharply defined plaques of sclerosis homologous to those found in the brain and cord were noted.

The following is a list of the recorded cases of the combined form of the two diseases, with abstracts of the clinical histories and pathological findings. There are seven cases in all, six with autopsy:

CASE I. (Schultze').—Man, aged thirty-six years. Syphilitic infection. December, 1876, onset with frontal headaches, pains in the extremities, and intention tremor. Diplopia; paræsthesia in the arms

FIG. 4.

Sclerosis bordering lateral ventricle. Weigert-Pal method.

and legs. Severe vertiginous seizure in June, 1877. Later, epileptiform convulsions. Paresis of right arm. Pupils unequal; good reactions. Weakness of vision without objective findings. Transitory aphasic attacks. Appearance of mental symptoms in October, 1878: Delirious, screams, strikes those about him; later, delusions of grandeur, followed by apathy, progressively developing stupor. Hæmatoma auris. Died December, 1878.

Pathological Findings. Marked atrophy and narrowing of the convolutions of the brain. Dilatation of the ventricular cavity. Epen-

dyma granulations. Systemic degeneration of the pyramidal tracts and columns of Goll. Multiple disseminated plaques of sclerosis in cord. Uniform thickening of the walls of bloodvessels and increase of the connective-tissue elements throughout the brain and cord.

CASE II. (Claus[2]).—Man, aged twenty-three years. Grandfather insane; father a tabetic. Early symptom, uncertain gait. Diminution of sight and hearing, followed by evidences of mental change. Articulation disturbed, but speech not scanning. The ataxia increased. Remittent paralysis of the legs. Progressive mental deterioration. Diagnosis: general paralysis of the insane.

Autopsy. Thickening of pia arachnoid, especially over the frontal and parietal lobes. Stripping the pia over this area attended by loss of substance. The frontal convolutions are narrow and atrophic, fissures flaring. Dilatation of the ventricular cavity. Disseminated patches of sclerosis in the brain, brain stem, and cord.

CASE III. (Siemens[3]).—Woman, aged twenty-two years; single; hereditary taint; venereal infection. Admitted to the asylum in the summer of 1876 with acute mania. During this attack, which lasted six months, it was noticed that the legs were handled clumsily. Later, mental enfeeblement, scanning speech, intention tremor, and ataxia. No nystagmus. Epileptiform attacks of short duration. In July, 1878, a relapse of the mania, lasting four months, followed by dementia. Pupils not mentioned.

Autopsy. Leptomeningitis and atrophy of the frontal convolutions. Partial sclerosis of the cerebellum. Disseminated plaques of sclerosis in the cord, none in the brain.

CASE IV. (Zacher[4]).—Man, aged fifty-three years. In the autumn of 1878 a fall, followed by headaches and backaches. A few months later excitable and irritable. Failure of memory. Admitted to the asylum July, 1879. Pupils unequal; reactions present. Articulation difficult. Ataxic gait. Sensation normal. Knee-jerks +. Marked dementia. Delusions of grandeur. Intention tremor. Epileptiform attacks. Speech inarticulate. Marked tremor of body.

Autopsy. Atrophy of convolutions, especially over frontal lobes. Ventricle dilated. Vessels of cortex are increased in number. Walls thickened. Multiple plaques of sclerosis in the cord.

CASE V. (Otto[5]).—Man, aged thirty-five years. Onset with progressive amblyopia, weakness and uncertainty of legs. Later, ataxia of arms and legs. Optic atrophy. Nystagmus. Scanning speech. Increase of the tremor and ataxia. Exaggerated tendon reflexes. Disturbance of the tactile sense. Duration of the above symptoms eight years, followed by progressive mental failure terminating in dementia. Duration of the disease, twelve and a half years. Pupils equal and reactions present throughout.

Autopsy. Pachymeningitis interna hemorrhagica over the frontal region. Pia arachnoid thickened. Marked atrophy of the convolutions of the frontal and parietal lobes. Numerous foci of disseminated sclerosis in the brain and cord. Sclerosis of walls of ventricle of cartilaginous consistency.

CASE VI. (Otto[5]).—Man, aged twenty-seven years. Early symptoms: Vertigo, headache, and dimness of vision. Later, ataxia, nystagmus, intention tremor, scanning speech. Failure of memory. Dementia.

Autopsy. Thickening of the skull over the frontal region. Atrophy of the convolutions. Disseminated plaques of sclerosis in the brain, stem, and cord.

CASE VII. (Petroff [8]).—Without autopsy.

Clinical Study. Dementia paralytica and multiple sclerosis. Man, aged forty-seven years. No alcoholic excesses; no syphilis. Onset October, 1896, following a fall. Difficulty in articulation. Occasional attacks of mental confusion. August, 1899, ataxia and intention tremor of the arms. Walking almost impossible. Tendon reflexes exaggerated. Speech scanning. Mentally confused and dull. Incontinence of urine and feces. Can neither stand nor walk. No nystagmus. Optic disks normal. In January, 1900, attacks of depression and excitement. Tremulous speech. Tremor of the tongue and face. Ankle-clonus. Pupils normal. In August, 1900, delusions of grandeur. He is the Kaiser, has much money, is wealthy, etc. Dementia is pronounced. Speech disturbance is a combined scanning with a *silben stolpern.*

REMARKS. The present case is put on record as representing the combination form of the two diseases, multiple sclerosis and dementia paralytica.

Although the symptoms of disseminated sclerosis were not apparent until the forty-fifth year, the cerebrospinal distribution of the lesions and their macroscopic and microscopic features were identical with those of the juvenile form, while the extent, character, and severity of the cortical degenerative process would correspond only to that observed in general paralysis of the insane.

Premature senility might be suggested as a possible basis for the mental symptoms and cortical atrophy.

The age of the patient (fifty years) almost precludes this theory. Premature senility is, however, rarely observed; but even this unusual occurrence could be excluded by the absence of the usual senile changes in the brain—*i. e.*, arteriosclerosis of the circle of Willis, encephalomalacia, pigmentation of the ganglion cells, corpora amylacea.

Diagnosis. The diagnostic difficulties encountered in such cases are considerable.

In the earlier stages of multiple sclerosis and dementia paralytica a certain resemblance is not infrequent, as many of the symptoms are common to both. Thus apoplectiform and epileptiform attacks occur frequently in both affections.

Systemic degenerations in the posterior and lateral columns, so frequent in paresis, produce symptoms similar to those following a development of plaques in the same areas.

The nystagmus, scanning speech, and intention tremor when typically present leave no room for doubt.

But these important symptoms of multiple sclerosis are sometimes absent, or occurring in an atypical form may simulate the hand tremor

and speech disturbance of paresis. On the other hand, typical nystagmus and intention tremor are rarely observed in paresis.

The Argyll-Robertson pupil if present may justly be interpreted to indicate paresis—with some reservation, however, as this symptom is rarely met with in multiple sclerosis. Uhthoff[7] in an analysis of one hundred cases of *sclérose en plaques* found the Argyll-Robertson pupil once, and in four cases myosis with sluggish light reactions. In well-marked cases of either affection errors in diagnosis would hardly be possible.

When the two diseases are combined the diagnostic difficulties offered are very great. In none of the recorded cases with autopsy was the combination form recognized clinically.

Usually in the earlier stages the condition was diagnosed as multiple sclerosis, but with the advancement of the mental symptoms the diagnosis of paresis was substituted.

It has happened that the clinical picture from the first has been that of paresis, the plaques of sclerosis being unsuspected until demonstrated by autopsy.

Cerebral Type of Multiple Sclerosis. In the advanced cases of pure disseminated sclerosis the lighter grades of dementia are not uncommon; this is usually attributed to an increase of the sclerotic process in the brain.

Some cases show early in their course symptoms of mental failure which advances rapidly to complete dementia. This is caused by a rapid extension of the sclerotic process in the brain (cerebral type of multiple sclerosis).

In such cases hallucinations, delusions, maniacal outbursts, attacks of melancholia, and delusions of grandeur are not uncommon. Here the pathological lesion consists of an extensive dissemination of the plaques in both the gray and white matter of the brain coupled with more diffuse sclerotic changes. Cases of this description are not common, and have been recorded by Schüle,[8] Jolly,[9] Greiff.[10] Cases somewhat similar, but differing in that the sclerosis was diffuse, involving the brain *in toto*, have been recorded by Kelp[11] and Schüle.[12]

Cortical Gliosis; Optic Atrophy; Posterior Column Degeneration. Another group of cases described by Fürstner and Stuhlinger[13] is of interest as bearing on the types under consideration. Their description is based on four cases having a similar pathology and symptomatology.

The essential pathological change consists in a diffuse gliosis of the marginal layer of the cortex. The glia proliferation is not confined strictly to this layer, but projects above the surface as small, rounded prominences (granula and tubera), and dips down into the second and even third layer of cells.

The tubera often contain small cysts, and minute depressions are

seen in the cortex as a result of this cystic degeneration. The gliosis is more pronounced over the frontoparietal regions of the brain.

The cells of the cerebral cortex are fairly well preserved; where the process dips down among them they are compressed and undergo atrophy. The overlying pia is sclerosed and the skull is thickened.

In addition to the cortical changes, in all the cases there was optic atrophy and systemic degeneration in the posterior columns of the cord. The authors refer the gliosis to lymphocytes originating from the bloodvessels.

In all the cases an hereditary taint was traceable, with evidences of a defective nervous system in early life (imbecility, intellectual weakness, and in one case epilepsy).

In two of the cases the symptoms of amaurosis and tabes preceded cerebral symptoms by a considerable time.

The speech disturbance resembled that of paresis with a scanning element. Facial, tongue, and hand tremors were present.

Mentally the picture was that of a progressive dementia, lacking the intensity, however, of the paralytic dementia.

Although this condition clinically would simulate most closely a dementia paralytica complicated by tabes and optic atrophy, it might well resemble the groups of cases under discussion, and deserves to be recalled and emphasized in this relation.

To summarize briefly, a clinical picture characterized by a progressive mental enfeeblement, manifesting during its course other symptoms of mental alienation, as mania, melancholia, hallucinations, and delusions, and accompanied by the somatic signs of multiple sclerosis, may be caused by the following pathological changes:

An extreme cerebral manifestation of the sclerotic process, of the same nature histologically as the disseminated plaques in the cord.

A combination of the two diseases, general paralysis of the insane and multiple sclerosis, in the same subject.

The diffuse gliosis of the cortex with optic atrophy and degeneration of the posterior columns also arises for consideration in the differential diagnosis.

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TUMORS OF THE SIGMOID FLEXURE.[1]

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For a long time my attention has been directed to tumors situated in *the left iliac fossa*—that is to say, *of the sigmoid flexure*—because occasionally there are to be found in this region palpable tumors the character of which is not easily recognized. May it therefore be permissible to give you a general review of tumors of this region? The most frequent occurrence of such tumors, which are *fecal accumulations*, present but small difficulty in diagnosis. They are easily recognized because of their comparative softness and because they not only occupy the descending colon, but also the rectum, where they may be easily felt by the examining finger. If in all doubtful cases you make repeated examinations after having thoroughly cleansed the bowels by laxatives or enemata, you will probably not be subjected to mistakes. The diagnosis becomes much more difficult with *the continuous presence of a tumor*. We must take under consideration intra-intestinal and extra-intestinal tumors, which may arise either from the pelvis, peritoneum, retroperitoneum, or the genito-urinary organs. The tumors may be new-growths, hard, or may be brought about by inflammatory swellings or by an abscess.

Of the *solid tumors* the most frequent are the carcinomata of the sigmoid. I say of the sigmoid, because I will only speak of the carcinomata confined to the sigmoid flexure and not of those of the rectum, which may extend upward. The recognition of the latter is not difficult when the physician, as a duty, will examine the rectum in every case where the symptoms point to disease of this part. It is not necessary for me to emphasize the latter point before you, members of this society, but rather to the general practitioner who frequently fails to do this. These cases are common enough where patients for a long time complain of dyspeptic symptoms and so-called hemorrhoidal bleeding, without the attending physician deeming it worth while to make

[1] Read before the American Gastroenterological Association, at Washington, May 14, 1903.

either a digital or speculum examination of the rectum. On this account patients are treated for a considerable time with different drugs and the best time for operation is lost.

Not long ago I saw a patient who was sent to the Riviera for neurasthenia and general anæmia, when at the first examination I found a carcinoma of the rectum. A most excellent rectal speculum is that of Otis, which was modified somewhat by my assistant, Dr. Küttner, so that it is introduced with considerable ease.

When the carcinoma in the sigmoid *is slow in its development* and grows to the outside, it is not difficult generally for diagnosis. The patient has in the beginning slight disturbances in his stools; there may be constipation alternating with watery or mucous discharges. Such discharges are characterized by the fact that astringents or opiates, either internally or by suppositories, do not affect them. The stools become tape-like; there may be discharge of bloody masses or pure blood may coat the stools, often combined with glossy mucus; however, the stool may look entirely normal in shape and color and, nevertheless, contain blood. It is of the utmost importance in such stools to see whether the blood is macroscopically within the feces by cutting through them, or this can be determined by chemical examination.

I have sometimes seen stools which were well formed and brownish-yellow in color, and without apparent abnormality, show with the Guajai test and other reactions undoubtedly large amounts of blood. When the growth degenerates, then the discharges contain a large amount of bloody material, with a foul odor. Simultaneously there develops a more or less painful cylindrical tumor in the left iliac fossa or distributed in nodular masses upward against the crest of the ilium. There is but slight tenderness or pain subjectively, and the general health is not markedly attacked.

When the growth is small and annular, the palpation may be fruitless when the abdomen is rigid and the patient is not yet emaciated.

Under such circumstances, after examination in a warm bath, in which the abdominal walls become relaxed, or after insufflation of the intestine, the diagnosis is made somewhat easier. When this is of no avail, and if in addition the general condition is not much changed, the whole complex seems to speak against a carcinoma of the colon. For the diagnosis, then, there remains nothing but the changes in the character of the stools or of the other functions of the bowel. One such case I saw in a patient in whom I diagnosed a carcinoma of the sigmoid flexure four years before his death, because of continuous irregularity of the stools and discharge of blood, without originating from any known focus. During one of my vacation trips the patient was examined by another well-known authority, who disputed my diagnosis because

of the good general condition of the patient. However, my opinion was confirmed by the autopsy. Most suspicious for such cases is the fact that there is a constant loss of weight for which there is no known cause; the appetite remains good; there is no vomiting and no local pain.

In many such cases obstruction suddenly occurs, with all its characteristic symptoms. Often the physician believes he has an intestinal strangulation, volvulus, or intussusception to deal with, whereas on operation a tumor is seen to be the cause. Such an accident happened to the celebrated French clinician, Potain.

Another group of cases are those in which the neoplasm grows into the lumen of the intestine, drawing the outer wall into it, causing no thickening and being hardly possible to palpate. Also such growths for a long time may lead to but slight symptoms or no symptoms at all. Suddenly there may occur an obstinate constipation lasting for several days, but relieved by laxatives and cathartics. Under such circumstances we have already a narrowing of the lumen, which becomes blocked by a fecal cork. Such attacks may repeatedly recur until finally cathartics, etc., are of no use. Distention of the abdomen may occur, but not necessarily confined to the descending colon. The general condition in these patients is but slightly affected in comparison to those cases of acute obstruction in strangulation, hernia, intussusception, etc., and the symptoms of ileus, such as fecal vomiting or fecal contents of the stomach occasionally emptied through the stomach-tube, are never present. In one of my cases, the continuous passage of gases pointed to an incomplete obstruction. Notwithstanding that no tumor could be palpated and that symptoms apparently began suddenly with an acute ileus two days before admission to the hospital, I diagnosed carcinoma of the sigmoid flexure because of the following: 1. During the past year there were four attacks of constipation with pains. 2. Moderate distention of the abdomen and more marked distention in the left iliac fossa. 3. Moderate pain in this region, both subjectively and objectively; the pain recurred on some days at regular intervals of ten to twenty minutes, lasting one to two minutes and radiated outward from the sigmoid. 4. Rectum negative. 5. Neither water nor air could be introduced in large quantities into the intestine by the rectum. 6. The general condition of this fifty-seven-year-old patient was but slightly changed; pulse 60, normal in quality; urine contained indican; stomach contained no fecal masses. 7. For two days, despite all means, no passage of stool, but occasional passage of gas. The operation showed a circular carcinoma, which occluded the whole lumen of the sigmoid and allowed but a corkscrew-like channel large enough to admit a knitting kneedle.

But all of these tumors, when they have symptoms, are comparatively easy to recognize. Much more difficult is the next group of cases

which I shall now speak of. Under normal conditions we are able sometimes to feel the cord-like descending colon or the sigmoid flexure, which may be tender to vigorous palpation, when the abdominal walls are thin and relaxed. The cord-like feel disappears when the colon is emptied or inflated. When there are no symptoms of any intestinal disease it is not difficult to diagnose the character of such a tumor-like resistance. It is entirely different when there is a spastic contraction of the colon simultaneous with other symptoms, such as obstipation, irregular movements, pain and disturbance of the general condition. Under such circumstances we are compelled more to think of a malignant growth. When the spasm disappears after a specific therapy, such as suppositories of belladonna and morphine or small injections of oil or of chamomile tea with a few drops of tincture of opium, the tumor also disappears. Such spasms may occur as a pure neurosis, either as a sequel to irritation of the cœliac plexus or as a symptom of spinal-cord irritation, or in tabes or basilar meningitis. It may also occur in hysteria or as a reflex in inflammatory or ulcerative conditions of the neighboring organs and other parts of the intestinal tract. This latter can occur in inflammation or ulceration of the rectum, as in fistulæ, syphilitic ulcers, and ulcerating hemorrhoids. It may also occur in dysenteric and tuberculous processes. When the character of the stools and the general condition is similar to that in carcinoma, then there is a strong liability to mistaken diagnosis. To illustrate this I shall mention the following:

The patient, a man aged thirty years, who, up to eight days before admission into the hospital, gave in the history that he was always in fairly good condition. On examination, in the left iliac fossa was found a hard, cord-like tumor, which was believed to be a neoplasm of the sigmoid. The tumor mass was quite tender, whereas the ascending transverse and beginning descending colon were not at all tender to touch. Neither digital nor rectoscopic examination disclosed anything abnormal in the rectum. The somewhat reddened mucosa covered with mucus was without any defect. On inflating the colon, although only a small amount of air could be injected, the patient complained of severe pain and the tumor remained unaltered. During his first days in the hospital, under oil injections, the stools, were soft, brown, with but little mucus, blood, or pus. Evening temperatures were 103.6° to 103.8°. On the eighth day of his stay laparotomy was performed, and we found the colon thickened and somewhat hard, but no tumor was present. The serosa was smooth and glossy, and owing to the frequent muscular contraction the serosa was at regular intervals drawn inward, giving the colon the appearance of a screw. Adjacent to the colon were a number of slightly swollen glands. The nature of the process within the intestine could not be at this time determined. A new-growth of the intestinal wall was not possible to exclude; more likely it would be possible to think of a tubercular process or a dysentery, but least pointed to the latter. The operator

excluded the whole colon and made an anastomosis by means of a Murphy button between the cæcum and a very low part of the sigmoid. For two days after the operation the patient did very well and passed no blood in the stools, but on the third day he went into sudden collapse and died. Autopsy showed the operation to be perfectly successful and no peritonitis. The whole colon from the middle of the transverse portion to the flexure showed a dysenteric condition present, but most marked in the flexure.

Even though the age of the patient spoke against carcinoma, the fact that such a distinct tumor could be palpated, the cachexia, the passage of very small amounts of mucus and blood, the glandular swellings, the absence of all symptoms of dysentery from the history, and his condition while in the hospital—all this was indicative enough to diagnose carcinoma.

It is also possible for a swelling of the colon to occur in the left iliac fossa *with a tumor in another portion* of the intestine. A distinct type of such a condition I was enabled recently to observe:

Man, aged sixty-nine years, who had the symptoms of a chronic ileus. In the lower left abdomen we could feel a cord-like tumor, hard but entirely painless, and apparently adherent in the lower part. In the knee-elbow position we were able to feel per rectum a number of small, pea-like nodules at the beginning of the sigmoid, lying apparently under the mucosa, and the intestinal wall at these points appeared thickened. The descending and transverse colon at times showed evidences of distention, at some times more marked than at other times. In the hepatic flexure was a hard swelling, and so movable that we thought of a movable kidney, but this swelling disappeared under massage. Subsequently the patient had fecal vomiting, and was operated on. To our surprise there was no tumor of the sigmoid flexure; in fact, this was entirely free and only a few slightly swollen retroperitoneal glands could be made out, which we felt through the rectum. However, an inoperable carcinoma of the hepatic flexure was found and a right-sided colostomy made. After this the distentions of the colon ceased and the patient felt so well that he left the hospital. Evidently the condition of the sigmoid was reflex to the presence of the neoplasm of the hepatic flexure.

Such experiences lead to caution in the consideration of such tumors. Not long ago I was seen by a patient who was practically prepared for operation. Another physician had diagnosed a carcinoma of the sigmoid and advised immediate operation. A tumor could readily be palpated in the left iliac fossa and the patient passed blood in his stools. On close examination, however, the stool was of good form and only covered in its outer surface with blood. The interior of the stool contained no blood. Under chloroform narcosis the tumor disappeared, and with the aid of the Kelly proctoscope I was able to detect one highly situated bleeding, hemorrhoid. This was cauterized at this time, and all bleeding ceased. The best evidence that the tumor was not due

to a neoplasm is that the patient within the last half-year gained more than eight pounds in weight. Some time ago I published a series of cases and showed that such hemorrhages from highly situated hemorrhoids could be the source of continuous bleedings and severe anæmia, the real cause of which is not detected. When the blood is passed with the feces and is not visible, the true condition remains unrecognized and pernicious anæmia is thought of.

There are, of course, other tumors in this region, such as those originating from the uterus and appendages, from local peritonitis, intussusception, etc. These conditions I will not discuss because under careful examination they are easily recognized. I would much rather speak of autointestinal intoxication as a result of marked constipation of long standing. In 1896 Herter and Smith[1] published a very complete investigation concerning excessive intestinal putrefaction, in which they proved that in cases of dyspeptic and neurotic individuals the presence of ethereal or aromatic sulphates in the urine were decidedly increased, so that the relation between the preformed sulphates and ethereal or aromatic sulphates was much altered. Under normal conditions the ratio between the two is 1 to 14, whereas in autointestinal intoxication the ratio may sink to 1 to 5, or even lower.

I will not speak of the more chronic cases as described by Herter and Smith or by McCaskey,[2] but will mention a group of cases which are acute in onset, very severe in their appearance, and accompanied by a more or less diminished sensorium of the patient. There may occur a paralysis of the extremities, complete absence of patellar reflexes, involuntary micturition and defecation; the whole picture strongly resembles a severe central brain disease. It is to be differentiated from brain disease by the bilateral paralysis, from meningitis by the absence of rigidity of the neck and the absence of the pupillary symptoms, and from disease of the spinal cord by the occasional occurrence of coma. If we palpate the abdomen of such patients we can feel more or less distinctly several hard, fecal masses in different parts of the tract. Digital examination of the rectum reveals this to be widely dilated, owing to the presence of many solid, fecal masses, which are not affected by irrigation, but must be removed by the fingers or other mechanical means. At the same time succussion of the stomach is distinctly present and indicates an atony of the same. Of three cases I found *in one a dilatation* of the stomach, but no enlargement in the other two.

If, however, we use irrigations of lukewarm oil or of hot water, we can empty the rectum of thick, dark-brown, solid masses; and if at the same time we empty the stomach by lavage of any stagnating material,

[1] Observations on Excessive Intestinal Putrefaction. New York Medical Journal, 1895.

[2] Anæmias Secondary to Gastrointestinal Disease, with Report of Two Cases. Journal of the American Medical Association, March, 1902.

the whole picture becomes suddenly changed. Consciousness returns, the paralyses disappear, and in a few days there is a complete return to the normal condition.

There can be no question but that such attacks arise as a result of *absorption of toxic agents* produced by putrefaction in the intestinal tract. In two cases I determined the ratio between the preformed and aromatic sulphates and found the latter markedly increased. Whether there is any further change in the metabolism of the proteid molecules and the formation of diamin, or if there occur gaseous products such as sulphureted hydrogen, I will not dispute. I have continually endeavored to isolate from the stomach contents, urine, and feces these toxins, which I found formerly in one case of tetanus and dilatation of the stomach, but without result. They are either too small in quantity or are so changeable that with our present methods we are unable to detect them.

CONCERNING THE NATURE OF CERTAIN CASES OF CHRONIC POLYARTHRITIS.

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and

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During the last few years a number of articles have been published by Poncet, or by others under his guidance, in which there has been strong insistence upon a belief of Poncet's that some cases of chronic rheumatism, arthritis deformans, and even conditions that may readily be mistaken for acute rheumatism, are at times a form of tuberculosis of the joints—a possibility that has previously been casually suggested, only to be denied. Several years ago, while unacquainted with the articles by Poncet and his pupils that had then been published, one of us (Edsall), with the same thought in mind, began some observations on the effect of tuberculin injections in cases of chronic rheumatism and arthritis deformans. It was hoped that the tuberculin injections would provide a means of choosing certain cases for more detailed study, and would, perhaps, through the production of a severe local reaction, offer a certain amount of direct evidence of the truth of the theory. The opportunity to carry on these observations in any considerable number of cases did not present itself until the fall of 1902, when we continued the investigation conjointly, chiefly at the Philadelphia Home for Incurables.

We have now used tuberculin in eighteen cases of chronic polyarthritis —in part, arthritis deformans; the remainder, so-called chronic rheuma-

tism. The various classifications of cases of chronic polyarthritis used by different authors are so unlike and in some ways so confusing that our method of grouping cases perhaps needs explanation; we have, for the sake of some definiteness, used the main distinctions formulated by Pribram. In all but one of these cases, circumstances have limited our study to the usual methods of clinical investigation plus the effects of the tuberculin injections; in one case we have been able to obtain other important data. We believe that our results are sufficient to suggest that tuberculosis may be the cause of the joint disease in several of the cases; and in one case that will be described in detail the evidence in favor of this view is strong. In connection with the work of Poncet and his pupils, our results provide indication of the importance of determining in a large number of cases the actual relation that tuberculosis may bear to chronic polyarthritis. A definite decision can, of course, be reached only by direct histological and bacteriological study of the joints of a series of cases, and satisfactory opportunities to carry on such studies in a convincing manner are not often found and have not been afforded us. The most important difficulty in this is, of course, the fact that the subjects of chronic polyarthritis usually live for many years after their joint disease has made its appearance; and commonly when post-mortem examinations are made, the joint disease has long been quiescent and the factors originating it have probably ceased to act. If these were bacteria they have probably died.

Tuberculous disease of the joints as usually recognized is so different from either chronic rheumatism or arthritis deformans that one must at first be impressed with the thought that these conditions are essentially different in nature. It is not necessary to describe in detail their different characteristics; the chief of these alone are very distinctive.

Tuberculosis, in the great majority of instances, is monarticular, or, at most, oligoarticular; and when it progresses unchecked for any considerable length of time it nearly always exhibits its characteristic tendency to fungous growths, gelatinous infiltration of the periarticular structures, abscess, and sinus formation. Both arthritis deformans and chronic rheumatism, on the contrary, tend strongly toward the involvement of many joints; they very often cripple practically all the joints to some degree; and neither of them is associated with changes in the joints or in the periarticular structures that are in any way similar to those seen in tuberculosis. Chronic rheumatism cripples its subjects through progressive fibrous, or sometimes ultimate bony ankylosis, while arthritis deformans accomplishes its results through the combined atrophic changes in the cartilages and the bones and the periarticular bony growths. In the rare instances in which actively destructive changes occur in the joints in these conditions, they usually

involve only one or two joints, and are commonly looked upon as accidental complications.

There are, however, certain relations between joint tuberculosis and chronic polyarthritis that are somewhat suggestive. Among these are the frequent occurrence of pulmonary tuberculosis in the subjects of chronic polyarthritis, the very common family history of tuberculosis and the fact that the same general conditions of environment that favor the development of tuberculosis are recognized as frequent elements in the early history of chronic polyarthritis. Such facts alone constitute but weak evidence of the correctness of our position, but they have some weight when we consider that there are rarer forms of joint disease that are known to be tuberculous and that exhibit characteristics midway between these two groups; and the usual dissimilarity between joint tuberculosis and chronic polyarthritis is less imposing if these two classes of cases are brought into analogy with chronic lymphatic tuberculosis in its two chief forms. We now know that many cases closely simulating true pseudoleukæmia are really lymphatic tuberculosis; and the difference, both clinically and pathologically, between this condition and ordinary scrofulous glands is certainly quite as striking as that between ordinary tuberculosis of joints on the one hand, and the two chief varieties of chronic progressive polyarthritis on the other. Another somewhat analogous condition that is also worthy of mention, because it involves serous structures, is chronic multiple serositis.

This is, in a considerable proportion of cases, certainly tuberculous, though it often presents no distinctive clinical evidences of its nature, and it is often difficult to demonstrate at autopsy whether it is or is not tuberculous.

The points that have just been mentioned are those that led us to begin the observations that we are now recording. The reports of Poncet, Barjon, Berard and Destot, and Mailland have given us additional ground for active interest in the question. The facts of importance that have been brought forward by these authors are practically as follows: They have frequently observed the development of pulmonary or other clearly recognizable forms of tuberculosis in cases of chronic polyarthritis. In a number of cases they have noted the development of a condition that, clinically, was typical tuberculosis in one or two joints in subjects of so-called chronic rheumatism. In one instance the injection of fluid obtained by tapping such a joint produced tuberculosis in a guinea-pig; in several instances the injection of fluid or tissue from such joints, obtained post-mortem or through excision of the joint, produced tuberculosis in guinea-pigs. And, finally, Barjon and Berard and Destot, in a series of cases, secured skiagraphic pictures which they consider practically identical with those of tuberculosis of

the epiphyses, the pictures exhibiting the characteristic points of rarefaction in the ends of the bones.

Poncet and his students conclude from these results—somewhat hastily, we think—that they have established the fact that chronic polyarthritis is frequently of tuberculous nature. Their results scarcely justify so definite a decision. The skiagraphic pictures that they have published are suggestive, but not convincing; in fact, such a method of observation can hardly be entirely convincing. And the development of a condition that, clinically, seems to be tuberculosis of one or two joints, or even the bacteriological demonstration that one or two joints are tuberculous, does not constitute definite evidence that the disease in all the other joints is tuberculosis. It is, of course, possible for tuberculosis to develop in a small number of joints that are already the seat of chronic disease, purely as a complication of the original trouble, and such an occurrence does not demonstrate that the original polyarthritis was essentially tuberculous. Inoculations made from several joints that were not so evidently the seat of tuberculosis would, perhaps, have furnished convincing evidence of the correctness of Poncet's argument; but such a procedure does not seem to have been attempted, the inoculations apparently having been made solely from the joints that were clinically the seat of tuberculosis. The results of these observers are, however, extremely suggestive and deserve very serious attention.

Our own results in all but one of the cases reported are, at best, merely suggestive. In one special case we believe that the facts that we present constitute weighty circumstantial evidence. For the sake of brevity, we shall avoid almost all details in mentioning the individual cases, merely stating the general class to which each case belongs and the important facts relating to it.

Of eighteen cases injected with tuberculin, eight gave absolutely no reaction, three gave a doubtful reaction, and seven gave a distinct reaction. The main points about these cases are as follows:

Of the eight that did not react, all but two were typical arthritis deformans. Of the two exceptions, one (Case I.) was a chronic rheumatism of four years' duration in a man aged twenty-five years. There had been repeated mild exacerbations of the condition, and the disease had produced partial fibrous ankylosis of all the larger joints, except the hips, of the carpus and the tarsus, and of a number of the fingers. There was no evidence of bony change. The patient had no enlarged glands, and his temperature was constantly within the normal bounds. The other case not arthritis deformans (Case II.) was an obscure case of multiple hydrarthrosis of two years' duration in a man aged thirty-four years. This patient had no fever, no glandular enlargement, and there was no evidence of bony change. The condition was confined to the large joints.

Of the six cases of arthritis deformans that did not react, one (Case III.) occurred in a woman aged seventy-two years, was of three years' duration, had begun in the small joints, and had involved nearly all

the joints of her body. She occasionally had a rise of temperature up to 100° F., and the temperature varied irregularly between 97° F. and 100° F. She had bony grating in many joints and osteophytes about numerous joints. She had no noteworthy glandular enlargement, except one gland, the size of a hazelnut, in the left axilla. The second of these cases (Case IV.) was in a woman, aged seventy years, whose disease was of twenty years' duration. She had no irregularity of temperature and no glandular enlargement. The disease was characteristic, widespread arthritis deformans involving both small and large joints. Case V. was in a woman, aged seventy years, whose disease was of thirty years' standing and had produced typical advanced lesions of arthritis deformans. She had no irregularity of temperature and no glandular enlargement. Case VI. was similar to the last described; it was in a woman, aged seventy-two years, was of twenty-eight years' duration, and had produced advanced lesions. There was no irregularity of temperature or glandular enlargement. The seventh case was in a woman aged fifty-three. The disease had lasted twenty-seven years, had involved nearly all the joints, and had produced typical changes. Her temperature was always practically normal, and there were no glandular enlargements. The eighth case was in a woman aged fifty years. The disease was of twelve years' duration; it had produced extensive lesions and most remarkable atrophic changes in many of the joints, with very marked deformities. She had no glandular enlargement. She frequently had a rise of temperature to 100° F., or slightly higher; but this was probably due to an intractable bed-sore.

The three cases that gave a doubtful reaction were as follows: The first (Case IX.) was in a man, aged forty-two years, who had had chronic rheumatism with repeated febrile exacerbations for somewhat over two years. The disease had produced thickening about the tarsus on both sides. The ankles were partly ankylosed, and the knees, wrists, and one elbow were extensively diseased. The patient had no glandular enlargement. The injection of 3 mg. of tuberculin was followed by fever and severe joint pains; but, since this was immediately succeeded by a febrile course with renewed joint symptoms lasting for ten days, and since the temperature began to rise almost immediately after the injection, what was at first thought to be a reaction was probably merely an exacerbation of the disease. The patient soon disappeared from observation, and the injection could not be repeated.

The second case in which there was a doubtful reaction (Case X.) was in a man, aged sixty-six years, who had extensive chronic rheumatism, involving all the large joints except the hips and most of the small joints of the hands and feet, with effusion into some of the smaller joints. Three mg., 6 mg., and 10 mg., respectively, were given him at intervals of four days. His temperature varied irregularly from 97° F. to 99.2° F. ordinarily. The tuberculin caused no wider range of temperature; but after the injection of 6 mg. he complained of pain and soreness in all his joints, and after 10 mg. he had a general feeling of illness and intense pain in many joints. The joints presented no objective signs at these times. The man had a chronic cough, but had no tubercle bacilli in the sputum and no evidence of tuberculosis upon physical examination of the lungs, even directly after tuberculin had been administered. A number of axillary glands on both sides were

enlarged, some of them being at least three-quarters of an inch in diameter.

The third doubtful reaction (Case XI.) was in a man, aged thirty-one years, whose disease had lasted fifteen years and was of the type of chronic rheumatism, involving almost all the large joints and the majority of the small joints in the hands and feet. There was some effusion in several small joints, but no evident bony change. The patient's temperature had twice within a fortnight been recorded as high as 100.2° F. Three mg. of tuberculin were administered on December 7th, and forty-eight hours later his temperature reached 100.8° F. This had not been recorded, and 6 mg. were given the following morning, when the temperature was still somewhat elevated. The injection of 6 mg. was followed within twelve hours by an elevation of temperature to 101.4° F., the temperature gradually falling to normal within eight hours. There were no noteworthy subjective symptoms. This man showed marked enlargement of the axillary glands, several being an inch or more in diameter. The inguinal glands were quite large, and there were a few glands, the size of peas, palpable in the neck. The patient showed no evidence of pulmonary tuberculosis.

Of the seven cases that gave a distinct reaction to tuberculin, four were characteristic arthritis deformans, two were typical chronic fibrous rheumatism, and one was an instance of Still's type of chronic polyarthritis of childhood. Two of the cases of arthritis deformans presented some signs of apical disease of the lungs. In one of these cases the signs were extremely slight; in the other they were fairly definite. The reaction in these two cases is probably of no consequence in relation to the nature of the joint disease, as it is likely that the pulmonary trouble caused it. These two latter cases were as follows:

The first (Case XII.) was in a woman, aged fifty-three years, whose disease was of seven years' duration, had involved nearly all the joints, and had produced most curious and interesting atrophic changes. The patient had ordinarily a perfectly normal range of temperature. She had a slight contraction of the extent of resonance above the left clavicle, with some impairment of resonance. There were no auscultatory signs. She had enlarged glands in both axillæ, a number being the size of large hazelnuts; and there were several glands in the neck the size of large peas. The injection of 3 mg. of tuberculin caused a rise in temperature to 100° F., with a slight feeling of malaise. Six mg. produced a similar rise in temperature, with a general feeling of intense malaise, nausea, vomiting, and headache. The patient also complained of some soreness in a few of the joints; but this was not marked, and was accompanied by no objective signs.

The other case with pulmonary signs (Case XIII.) was in a woman aged thirty-two years, was of nine years' duration, and had produced characteristic advanced lesions of arthritis deformans. The axillary glands were enlarged, a few being as much as an inch in diameter; numerous cervical glands were readily palpable. Ordinarily she had no abnormal range of temperature. The injection of 3 mg. produced no result. Six mg. had no definite effect upon the temperature, but gave the woman a feeling of marked malaise and some general pain. Ten mg. caused a rise in temperature to 100° F., general intense malaise, nausea, and diffuse aching. She complained particularly of the pain

in several joints, which had previously been for a long time practically free from pain.

Of the cases with no pulmonary signs that showed a distinct reaction, one (Case XIV.) was in a woman, aged sixty-three years, whose disease was of twenty-seven years' duration. There was characteristic advanced arthritis deformans. Numerous axillary glands were readily palpable. The patient ordinarily had no fever. The injection of 3 mg. was followed by a rise in temperature to 100.2° F., some general aching pains, and a feeling of malaise. Six mg. given nine days later produced a rise in temperature to 101.2° F., general intense malaise, headache, and aching pains. She had no special joint symptoms at this time, and there were no objective changes in the joints.

Case XV. was in a woman, aged thirty-three years, whose disease was of four years' duration. It was typical arthritis deformans that had very rapidly advanced and had produced changes in almost all the joints, including the jaw and the spinal column. She had no abnormal range of temperature, no signs of pulmonary disease, and no glandular enlargement. The injection of 1½ mg. of tuberculin produced a rise in temperature to 101° F., with general malaise, but with no localized subjective or objective symptoms.

The sixteenth case was in a man, aged thirty-seven years, whose disease was of seven years' duration. It was chronic rheumatism that had involved most of the large joints and had produced irregular involvement of many small ones. His temperature range was ordinarily normal. He had no glandular enlargement, and no signs of pulmonary disease. His joints gave him no noteworthy active discomfort. Three mg. of tuberculin caused no rise in temperature; 6 mg. produced a rise to 100° F., with no general signs. Ten mg. caused a rise to 101.6° F., with a general intense feeling of illness, headache, nausea, and general aching pains. He had very marked pain in many joints, and a number of them became extremely painful and very tender upon palpation, these joint symptoms subsiding rapidly within twelve hours. He had no evidences of a reaction in the lungs.

The seventeenth case was in a woman, aged forty-four years, who had chronic rheumatism that had lasted for two and one-half years, and had involved the tarsus and carpus on both sides, both ankles, knees, and wrists, and the left elbow. She had no abnormal range of temperature, but had slight glandular enlargement in the axillæ and groin. The injection of 1½ mg. of tuberculin caused her temperature to rise to 101° F. There was also severe pain in the wrists and knees (the joints most recently involved), with a good deal of tenderness and of pain on moving these joints. This patient, however, was subject to frequent exacerbations of her joint symptoms.

The eighteenth case is the one upon which we would lay especial stress, and it will be mentioned in somewhat greater detail than the others. It was an instance of Still's type of chronic polyarthritis associated with marked glandular and splenic enlargement. The patient was a boy who before his admission to the Home for Incurables had been in the Children's Hospital under the care of Dr. Stengel and Dr. F. A. Packard. We have kindly been allowed to make notes from the records of the Children's Hospital:

When admitted to that institution in August, 1900, the boy was eleven years of age. He was ill-nourished, had been in very bad

hygienic surroundings, and had been ill-treated by his parents. He had no tubercular or rheumatic family history. He had had measles at the age of eight years, but no other illness up to the time that his joint trouble began, in March, 1900. The right ankle was first affected; then the right foot; next the left ankle and left foot. In June, 1900, the right knee had become involved; then the left; and in July both hands. There had been no severe acute symptoms; but the child's general health had gradually failed with the progress of the joint disease, and the joints involved had grown progressively worse.

When admitted to the Children's Hospital the patient's axillary glands were noted to be swollen and hard. The posterior cervical glands were not enlarged, but the epitrochlear and inguinal glands were palpable. The splenic dulness was increased. The main facts concerning the joints at that time are that the wrists were swollen and there was fluctuation over them; the finger-joints, especially the first and second phalangeal, were swollen and hard; the metatarsophalangeal joints of both great toes were swollen and tender; the ankles and the region over the tarsus were also swollen and somewhat tender; and the knees were enlarged, movement at the knee-joint causing pain. The blood examination showed 6,000,000 red cells, 14,000 leukocytes, and 60 per cent. of hæmoglobin. There was a systolic murmur over the pulmonary region of the heart. That organ was otherwise normal, except for a moderate accentuation of the second pulmonary sound.

The child remained under observation in the Children's Hospital until March 13, 1901, when he was sent to the Home for Incurables. During his stay in the Children's Hospital there had been repeated temporary exacerbations of the objective and subjective signs in the various joints, and it was repeatedly noted that increased glandular enlargement had occurred in regions corresponding with the joints that had shown active signs. The leukocytes were several times counted; after the first count they were found to be near 8000. The temperature was very irregular, mounting to 100° F., and frequently higher, sometimes up to 102.3° F., every day until September 4th. It was then nearly normal until October 2d. After this it ranged as high as 102° F., frequently for a week, and then remained nearly normal for two weeks. It was then elevated daily for a month to as high as 102° F. Similar variations in temperature were exhibited up to the time of the patient's discharge. It was noted that gentle massage of the joints was painful and seemed to increase the symptoms. He was discharged unimproved.

The notes upon his admission to the Home for Incurables were much the same as those that have been mentioned. When first seen by us, in July, 1902, he had improved in general nutrition. His joints remained much as they had been upon admission, though he had for some months had no pain in them, and no increase in other joint symptoms.

He had at that time very striking glandular enlargement. The anterior and posterior cervical glands were palpable in great number and were of various sizes, ranging up to the dimensions of a pigeon's egg. The axillary glands on both sides were very large, there being a number in the right axilla that were as much as an inch in diameter. In the left axilla there was one as large as a small hen's egg, and several with a diameter of about an inch. The brachial glands were

very readily palpated. A number of the inguinal glands were as large as a hazelnut. The splenic dulness was distinctly increased, but the spleen could not be felt. This was perhaps due to the fact that the boy's deformity rendered it likewise difficult to palpate the splenic region.

He had no definite signs of pericarditis, a frequent complication of this type of joint disease. He had likewise no other signs of cardiac disease, and no signs of disease of the lung; the abdominal signs were also normal. The joint conditions were as follows:

The jaw was unaffected. The head could be rotated but little, and was held bowed forward somewhat; there was but little anteroposterior motion. The lower cervical spine could not be felt to move. The left shoulder was practically free. In the right shoulder anteroposterior motion was moderately limited, and the arm could be abducted only about 30 degrees. There was no appreciable enlargement about the shoulder. At the left elbow the arm could be extended only a little beyond a right angle; it could be further flexed fairly well. The movements of the radius were fairly good. There was no enlargement of the joint. The right elbow was globose in appearance; it was held at about 100 degrees, and was almost absolutely fixed. There were no bony enlargements, but the whole joint was somewhat rounded from thickening of the soft tissues. Both wrists were held almost rigid at about a right angle. There was very slight motion in either. There was no noteworthy thickening about the wrist-joints themselves; but on each side there was marked swelling of the carpus and of the upper half of the metacarpus, particularly on the right. There was apparently some fluid on the right over the carpus, the swelling otherwise being due to thickening of the soft tissues; no bone enlargement was demonstrable. The carpal and metacarpal joints were rigid. The metacarpophalangeal joints on both sides showed very little motion, flexion beyond a straight line being practically impossible. The joints were held overextended, and were capable only of slightly greater extension. At the first and second metacarpal joints on each side there was marked thickening, which seemed to be partly of the ends of the bones. On both sides the first interphalangeal joints of all the fingers were thickened, this being especially marked in the left hand. The epiphyses of all the fingers of the left hand, and of the first two of the right hand were apparently thickened at this joint, and there was also thickening of the soft tissues. The middle, ring, and little fingers were flexed at about a right angle, and there was practically no motion in the interphalangeal joints. The first finger on each side showed a little more motion. The thumbs on each side showed thickening and apparently subluxation at the metacarpophalangeal joint. Both joints were almost entirely fixed, the last joint showing also some enlargement; this appeared to be in part of the bone.

Motion in the left hip was slightly limited; the right hip was practically free. The knees were globose in appearance. The ends of the bones felt somewhat enlarged, and there was thickening of the soft parts, with partial obliteration of the normal prominences. There was some fluid under the left patellar tendon. At the knees the legs were held at a right angle; they could be bent back somewhat farther on the thigh; they could be straightened only very little. The ankles showed decided limitation of motion. The ankle-joints looked somewhat globose, and the appearance of swelling extended over the tarsus and

metatarsus. There was no fluid in this region, but there was thickening of the soft parts, particularly over the tarsus. The tarsus and metatarsus were rigid. There was practically no involvement of the toe-joints. There was no definite bony grating in any joint.

The following is a skiagraphic report of Dr. H. K. Pancoast, who was kind enough to make a series of plates for us on May 4, 1903. Only the main points in connection with those joints that showed noteworthy lesions are mentioned.

Left Hand and Wrist. Dense adhesions are present between all the carpal bones and in the radiocarpal articulation. The same is true along the line of the carpometacarpal articulations, especially between the first and the second metacarpals, and between the trapezium and the trapezoid. There is apparently a slight subluxation at the ulnar side of the first phalanx of the thumb. There are well-marked adhesions in the latter joint as well as in the interphalangeal joint. Deposits are present in the other metacarpophalangeal joints, with a widening of the proximal epiphyses of the phalanges.

Right Hand and Wrist. The radiocarpal, carpal, and carpometacarpal joints present a similar appearance to those of the right hand; but the adhesions are denser. The proximal ends of the first phalanges show a decided widening, corresponding with the epiphyses. There is a loss of bony substance in the distal end of the second metacarpal. The same end of the third metacarpal is apparently worn away on the radial side where the proximal end of the phalanx is overdeveloped.

Right Elbow, Lateral View. The olecranon epiphysis is possibly more advanced in ossification than is usual at this child's age. There are dense adhesions between the posterior portion of the olecranon and the region of the olecranon fossa. The elbow is flexed at about 120 degrees. There is no loss of bony substance at this articulation. There are a few adhesions between the coronoid and the anterior surface of the humerus on this side.

Left Knee, Lateral View. There are well-developed adhesions between the patella and the lower femoral epiphysis, the patella being in relation with the latter only. The adhesions apparently involve both condyles. The remainder of the joint cavity is fairly clear. There seems to be a thickening of the articular surface of the upper tibial epiphysis. There is no apparent loss of bony substance.

Right Knee, Lateral View. There are well-marked adhesions between the patella and the femur and between the femur and the tibia; and the articular surfaces of the femur and the tibia show very marked thickening, this being much more pronounced than in the other knee. There is a decided increase in calcification at the epiphyseal line in the upper end of the tibia, as compared with the opposite side.

The Hips. Both hips show marked adhesions between the femoral head and the acetabulum, and marked thickening of the articular surface of the femur. The angles of the necks seem to be more obtuse than is normal. The necks are greatly thickened, and on the left side the infiltration may readily be seen to involve the capsule.

Since the time of the physical examination described above, the boy has shown gradual but very distinct improvement. He has put on flesh; his color is good; and many of the joints have decidedly improved, so that while he was confined to a roller-chair in July, 1902, he is now able to run about with rapidity on crutches and to walk about a little

without either crutches or cane. His knees and ankles, particularly, are much improved in motion; and the wrist-joints and some of the joints of the fingers show decided improvement. Except for the result of the tuberculin injections, he has had practically no pain in any of his joints during the last year, though he has occasionally felt stiff. The glandular enlargement has decreased to a very striking extent. There are two or three glands in the neck that are still as large as peas, but none larger; and except for these the cervical glands are now scarcely palpable. The glands in the right axilla have become moderately reduced in size. Those in the left axilla have greatly decreased in size, so that at the time they were extirpated at an operation to be mentioned the largest was about an inch and a quarter in diameter. The inguinal glands are distinctly smaller than they were.

During the early part of the year the boy still had some tendency to rises of temperature. The temperature was usually nearly normal, but would occasionally shoot up to 100° F., and rarely to 101° F. These rises of temperature were not accompanied by any other symptoms. The results of the tuberculin injections in this boy were as follows: On October 29th 1½ mg. were injected without any definite result. On November 5th, at 3 P.M., 3 mg. were given. On the 6th, at 3 A.M., the temperature was 101° F.; at 6 A.M., 102° F. It persisted at about the latter point for six hours and then gradually declined, reaching normal at midnight. The boy felt generally miserable. His joints, which had been free from pain for months, became quite painful, and he begged that his daily massage be omitted, as he felt that he could not stand it because of the tenderness of his joints and the pain on movement.

Because the patient had, under ordinary circumstances, a tendency to fever, another injection was given, on November 12th, at 9 A.M., the temperature meanwhile having been regularly below 100° F. At 3 P.M. the temperature was 100.4° F., at 6 P.M. 103° F. It remained at near 102° F. for twenty-four hours, and then rapidly declined to normal, remaining nearly normal for four days after this, when the regular temperature records ceased. With this last reaction the boy was nauseated, felt quite ill, and complained bitterly of intense pain and tenderness in a number of joints. The wrist and ankles were swollen, there was some redness over them, and movement of the joints caused intense pain. The glands were slightly tender, but there was no change in their size or consistency. The patient had no pulmonary signs during the reaction, and none could be discovered at any other time. Since this time the boy has had no active joint symptoms, and there has been a progressive tendency toward improvement under the use of very gentle massage and general treatment.

On March 28, 1903, Dr. Jopson removed the glands from the left axilla, securing eighteen of different sizes. They were strongly adherent to each other, to the sheath of the vessels, and to the surrounding connective tissue. The largest was somewhat over an inch in diameter; there were two about three-quarters of an inch in diameter; the others were much smaller. Their macroscopic appearance was in no way noteworthy. There was not the slightest gross appearance of tuberculosis, and the glands were of about the normal color and consistency. Dr. Ravenel kindly made sections and animal inoculations from these glands. Microscopic examination showed absolutely no histological

evidence of tuberculosis, the only noteworthy changes being enlargement of the Malpighian bodies, the cells in which stained rather poorly; these changes were not striking. Several sections were examined for tubercle bacilli, but none were found.

The inoculations were made from an emulsion of several of the largest glands, this emulsion being of a consistency just sufficient to allow of its passing through a hypodermic needle. Five c.c. of it were injected into each of two guinea-pigs. The emulsion was stained with carbol-fuchsin, and a large number of acid-fast organisms with a perfectly typical appearance of tubercle bacilli were readily discovered, some of them lying singly or in twos, others forming quite numerous, fairly large clumps.

To our surprise, the result of the inoculation of the guinea-pigs was entirely negative. The animals remained well for five weeks thereafter, when they were killed. Dr. Gilliland, in the absence of Dr. Ravenel, kindly examined them. Most careful search showed absolutely no evidence of tuberculosis or other disease.

The fact that the acid-fast bacilli in the glands were tubercle bacilli cannot well be doubted, particularly in view of the response to tuberculin. The result of the inoculations shows that they must have been either dead or of extremely low virulence. Dr. Ravenel believes that they were dead, for they were present in large numbers, and a great many must have been injected into each guinea-pig in the 5 c.c. of emulsion. It is, of course, possible that some of them were dead and that some were of low virulence and still living. Naturally, this point cannot be definitely settled.

Conclusions. The observations just noted indicate that the boy whose case has just been discussed has tuberculosis. We believe also that the intense local symptoms in the joints after the tuberculin injections; the fact that the glandular enlargement has been so distributed as to be in apparent relation with the joint disease; that much of the glandular enlargement is known to have occurred after the onset of the joint disease; and, finally, the fact that the glands have several times been noted to be enlarged or decreased in size in accordance with the progress of the joint disease, all indicate that the joint disease stood in close causative relation with the glandular enlargement, and that both were produced by the same factors. If the joint disease is tuberculous it would seem that it must be of an even lower degree of virulence than ordinary joint or bone tuberculosis.

As to the more general conclusions to be drawn from our observations, we consider, in the first place, that this last case indicates that it is probable that a certain proportion at least, perhaps a large proportion, of the cases of chronic polyarthritis of the type described by Still constitute a peculiar form of tuberculosis of the joints. This seemed to us a very definite possibility, even before we observed the facts presented concerning this case, for children with this form of polyarthritis usually exhibit irregular fever and have striking general glandular enlargement—conditions that, without any disease of the joints, would provide

the main characteristics of chronic lymphatic tuberculosis of the Sternberg type. It does not seem wholly probable that all cases of this type are tuberculous, but this is a point that cannot wisely be discussed without further observations.

As to the other cases recorded, the effect of tuberculin can be considered to be of decided interest in but three instances, in the sixteenth and seventeenth cases and in the tenth case. The latter has been mentioned as giving a doubtful reaction, but it was doubtful only in the fact that the patient had no fever. He had such marked pain and tenderness, and such distress on moving his joints after 6 mg. and 10 mg. of tuberculin had been injected, that the probability that this was a local reaction without a general reaction is strongly suggested. The sixteenth case presented a striking set of joint symptoms at the time of the reaction, without any other marked general symptoms. The joints became both painful and decidedly tender, while the man had for a long time previously had but slight symptoms in his joints even with other acute illnesses. In the seventeenth case the severe joint symptoms produced by the reaction were of somewhat doubtful consequence, because the woman had been so subject to exacerbations of her joint pains. The symptoms were, however, extremely marked and very suggestive. The reactions obtained in the other cases must for the present be considered as probably of little importance, either because of the probable existence of pulmonary tuberculosis, or because of the absence of accompanying joint symptoms.

We are aware that joint pains sometimes accompany a tuberculin reaction even when disease of the joints is absent. We also admit that in persons who are already the subjects of joint disease, joint symptoms are more likely to be produced by any temporary disturbance of health than in those whose joints are free from disease. We likewise grant that a tuberculin reaction is not an infallible indication of the existence of tuberculosis; that it, at best, indicates only that tuberculosis exists somewhere in the body of the patient reacting, and does not usually demonstrate anything concerning any particular tissues; and it is extremely easy to overlook clinically some focus of tuberculosis in the lungs or in some other common seat of the disease. Hence, the mere development of a tuberculin reaction in a chronic joint case cannot, of itself, be considered to mean much, even though there are fairly striking joint symptoms at the time of the reaction; and we have no desire to draw any definite conclusions from these reactions. At the same time, we believe that the observations made in our eighteenth case render it quite possible that the reactions in those other cases which have been especially mentioned were due to tuberculosis of the joints. It is somewhat interesting that all but one of the cases reacting showed a noteworthy degree of glandular enlarge-

ment, and in none of the cases upon which stress has been laid could any evidence be found of the existence of tuberculosis of the lungs or of any tissues other than the joints or glands. The presence of chronic glandular enlargement of considerable extent and without other demonstrable cause is, in the present state of our knowledge, itself strongly suggestive of the possible presence of tuberculosis. It is, of course, possible that these patients reacted because they had tuberculosis of the glands and not of the joints; the facts that we possess do not permit of a decision on this point. We may, however, properly direct attention to the fact that all cases that we have mentioned with some emphasis showed severe joint symptoms at the time of the reaction, while none of them showed more than very slight tenderness of the glands. A recognizable local reaction in tuberculous tissues is common enough to make this point suggest that, in case both the joints and glands were tuberculous, the joints were the seat of a more active process.

In case tuberculosis proves to be a factor of importance in the etiology of chronic polyarthritis, it seems probable that cases due to this cause will be found chiefly in the group commonly classed crudely under the term chronic rheumatism. All our own most suggestive cases were of this class. It does not seem proper, however, to dismiss the possibility that arthritis deformans may be due to tuberculosis quite as brusquely as does Pribram, who admits the possible truth of Poncet's argument regarding chronic rheumatism, but disposes of it with a word when discussing arthritis deformans. Pribram's chief argument is that the radiographic pictures of tuberculosis are absent in arthritis deformans. We have previously stated that we do not believe that this method can offer final evidence of the presence of tuberculosis; we are equally convinced that it cannot positively demonstrate the absence of that disease. We know, for instance, that the microscope cannot conclusively settle this question with lymphatic tissue; hence it is improbable that the X-rays can do so with bone. Some of the more active cases of arthritis deformans that show febrile exacerbations and marked depression of the general health may, quite as properly as cases of chronic rheumatism, be studied from this standpoint. Should a considerable number of cases of chronic polyarthritis of any variety be shown to be tuberculosis of the joints of a peculiar form, it would be an important step toward clearing up our present uncertain knowledge of these conditions.

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CLINICAL LECTURE ON THE SYMPTOMATOLOGY AND TREATMENT OF TRIFACIAL NEURALGIA.[1]

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I want to call your attention to-day to some of the salient features of trifacial neuralgia, or tic douloureux—painful spasm—dwelling especially upon the clinical history and upon the indications for and the methods of treatment, prefacing my remarks with a brief reference to the etiology and pathology of the affection.

Etiology. It must be assumed that in every case the fundamental cause lies in some structural change, either central—that is, in the Gasserian ganglion; or peripheral, in one of its divisions. In a small percentage of cases we are able to single out certain conditions between which and the lesion itself the relation of cause and effect is easily proven. Thus, for example, there are sources of peripheral irritation, in many cases infectious, such as herpes, or some lesion of the teeth and gums, which give rise primarily to a peripheral neuritis, and secondarily to neuralgia. On the other hand, and in by far the large majority of cases, we are bound to admit that the essential cause is either hypothetical or absolutely unknown; but there are certain systemic conditions which, by virtue of the fact that they are sometimes the forerunner of this disease, have been regarded as "predisposing" causes. In this class we may include exhaustion hemorrhage, overwork, and strain; some forms of neurosis, as migraine, diabetes, chronic nephritis, gout, rheumatism, and lead poisoning. We know that women are attacked about twice as often as men, and the great majority of cases occur after the period of middle life.

Pathology. Not a great deal is known of this phase of the subject because, as yet, few opportunities have been offered the neuropathologist to make careful histological studies of specimens from individuals so affected; but from our present knowledge it can be positively asserted that there are two or three separate and distinct types of tic douloureux—one in which the lesion is primarily a neuritis of the peripheral branches, which subsequently may or may not extend to and invade the ganglion; the other, in which the primary lesion first appears in the ganglion; and a third, perhaps, in which the lesion is neither in the ganglion nor in its branches, but in the central nervous system. The lesion may be of a degenerative type, an interstitial neuritis or a neoplasm. Were the clinician able to recognize in his cases symptoms

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which would justify a classification corresponding to that of the neuropathologist, the indications for treatment would be more clearly defined. If the lesion was a peripheral neuritis, resection of the nerve trunk would be clearly indicated—a central operation would be unjustifiable; if, on the other hand, the lesion were primarily centrally situated in either ganglion or sensory root, the futility of the peripheral operation would be apparent.

Symptomatology. It would not be amiss here to remind you of a few facts concerning the anatomy and physiology of the fifth cranial nerve, or, as it is sometimes called, the trigeminus. It arises by two roots, a motor and sensory, the latter very much the larger. At the apex of the petrous portion of the temporal bone the fibres of the sensory root form a semilunar ganglion, the Gasserian ganglion. From the anterior border of this structure are given off three branches—the ophthalmic, the superior maxillary, and inferior maxillary; the first two divisions are pure sensory roots, but the third receives fibres also from the motor root. The motor root supplies the muscles of mastication, and the sensory root the skin of the face, the mucous membrane of the mouth and nasal cavity, the conjunctiva and cornea, and anterior part of the tongue with gustatory fibres. When the first division is involved the "tender points" will be found at the supraorbital notch, in the outer part of the upper eyelid, and at the emergence of the nasal branch at the lower edge of the nasal bone; the pain radiates over the anterior half of the head, to the eyelid and eye itself, and to half of the nose; the second division gives off a few branches as it traverses the sphenomaxillary fossa and appears at the infraorbital foramen as the infraorbital nerve, where it divides into the palpebral, nasal, and labial branches. When this division is involved the "tender points" will be found at the infraorbital foramen, at the side of the nose, and over the most prominent portions of the malar bone. If the dental branches are involved pain will be referred also to the teeth and gums of the upper jaw. Finally, if the third division is involved pain will be referred to the distribution of one or all of its sensory branches; to the parietal eminence, temple, and external ear (temporal and auricular temporal branch), to the tongue (lingual), to the gum and teeth of the lower jaw (inferior dental branch), and to the lower lip (mental branch). The tender points are at the inferior dental foramen, where the auriculotemporal crosses the zygoma, over the parietal eminence, in the tongue, and at the mental foramen. This colored diagram, to which I direct your attention, differentiates from one another the cutaneous distribution of each of the three divisions.

Now, the particular group of symptoms exhibited by any individual case will depend upon whether the ganglion or one or all of its divisions are affected. In the vast majority of cases tic douloureux is a

disease of the second or third divisions. It often affects either one of these divisions alone, for a long period of time, although eventually it may extend to the other, but it is extremely rare for it either to begin or to remain localized in the first division. One of the patients, which I will show you to-day, suffered from this exceptional form of the disease. When he first came under my observation he was sixty-eight years of age; he had been a hard worker ever since he was ten years of age. He was not given to excesses of any kind. He himself had inherited no tendency to neuralgia, but one son and one daughter were subject to attacks of infraorbital neuralgia. About five years ago he first began to have sharp, shooting pains, referred to the course and distribution of the right supraorbital nerve. During the past four years on four different occasions the supraorbital nerve was divided, and in one instance a considerable section was resected, but after each operation the pain returned. After the first operation he enjoyed relief for about a year, but after each succeeding operation the period of relief was always shorter. I recite the history of the case chiefly because it illustrates this unusual type of tic douloureux in which the pain not only begins but remains localized in the first division. But the history of this case illustrates two other points equally instructive, but more commonly observed in this class of cases—I refer to the necessity for repeated peripheral operation, and to the gradual diminution of the period of relief after each successive operation. By far the great majority of patients that come under our care have already had a number of peripheral operations; they have become discouraged by the necessity for frequent recourse to operation, or, because the last operation afforded little or no relief, and plead for some more radical operation, no matter how desperate it may be.

Probably in the majority of cases of true tic douloureux you will be told by the patient that the pain began and was for a time restricted to the third division, and especially to its inferior dental branch, but that subsequently the remaining branches of the third division and the second division became affected. Last November Dr. Mills referred a patient to me whose history was more or less typical of this variety. The patient first complained of pain in the lower jaw, referred to the gums and teeth; believing the pain to be due to some disturbance at the roots of the teeth, the careless dentist recommended extraction, and one by one all the teeth of the right side of the lower jaw were extracted, but, as you would expect, without any relief. In the course of time the pain became more widespread and was referred to the mental and other branches of the third division. In the ward there is a patient upon whom I operated only a few days ago, whose history is very similar.

I have told you a good deal about the seat and distribution of the pain, but what of its character and intensity? In the first place, as in the

neuralgias of other nerves, the pain is spontaneous and paroxysmal. The paroxysms may be brought on by draught or exposure, by fatigue, emotion, and movement; for example, opening the mouth. During the paroxysm the pain is sharp, stabbing, or darting, and occurs every few minutes; a series of these successive pains constitute a paroxysm, and several paroxysms an attack. As to its intensity the pain of trifacial neuralgia is in some cases the most agonizing of all with which man is ever inflicted. Victims of the severe type of tic douloureux are the objects of greater commiseration than any other class of patients. Sometimes they become so crazed with suffering as deliberately to take their lives. There is the widest variation in the frequency with which attacks recur; there may be an interval of only a few hours or several months. Usually as time goes on the attacks increase both in frequency and severity. There can be said to be no periodicity, except in those cases in which the neuralgia is of malarial origin, or in those cases in which the attacks occur only during the catamenial periods.

During the intervals the characteristic pains of the paroxysms cease, but the patient is not altogether free from suffering. He may complain of a dull pain in the distribution of the affected nerve, and pain may almost always be elicited by pressure over the so-called "tender points."

Associated with these sensory disturbances there may be certain motor, vasomotor, and trophic phenomena; we see sometimes convulsive movements of the muscles of the face (motor disturbances), lacrymation, salivation, flushing, sweating (vasomotor disturbances), certain erythemata, loss of hair, and loss of hair pigment (trophic disturbances).

Classification. It will be of great assistance to one considering the question of treatment to have clearly set forth in his mind a suitable classification of the various types of the trifacial neuralgia. We have already alluded to three classifications: (1) a classification based on the seat of the lesion, ganglionic or peripheral; (2) a classification based upon the distribution of pain, whether in the distribution of the first, or the second, or the third divisions alone, or in two or all three of these divisions; (3) a classification, as suggested by Dana, which recognizes two types—one, the migrainous type, occurring almost always in women in early life, suffering from migraine; after a number of years it becomes chronic and becomes more localized, settling in the second or third or all three divisions. Dana considers this type to be an evolution of a definite trigeminal neuralgia on the basis of a migrainous neurosis. In the beginning it is a disorder of the sensory neuron, neither in the ganglion or its branches, but later certain degenerative changes may develop in the peripheral branches. The second type, and the more common of the two, affecting man as well as woman, occurs after the age of forty years, and is due to a definite lesion either in the ganglion itself or in its branches.

TREATMENT. With this brief summary of the symptomatology we may proceed to the subject proper of the hour, namely, the treatment. First of all, what resources have we upon which to draw or what courses have we to pursue? Generally speaking, they may be summed up under two headings: the medicinal or non-operative, and the operative. The question is naturally propounded—when is the one admissible, the other inadmissible, justifiable or unjustifiable, indicated or contra-indicated? In answering this question the following factors must be weighed and considered: (1) the duration of the disease; (2) the frequency and severity of the attacks; (3) the causes of the attacks: (*a*) whether known or unknown; (*b*) whether removable or not.

It may be asserted that, at the onset at least, the treatment of all cases of trigeminal neuralgia belongs to the domain of medicine rather than surgery—according to Dana the migrainous type should never be subjected to operation, because the lesion lies not in the peripheral branches or in the ganglion, but in the central nervous system. Upon what grounds, you may ask, do we base our assertion that in its incipiency at least the treatment of trifacial neuralgia should be medicinal or non-operative rather than operative? Because clinical experience teaches us that by these means in a certain percentage of cases the disease may be arrested, if not permanently, at least for long intervals; furthermore, that in some cases the disease has a tendency to run its course, usually reaching its height in five or six years, and then exhibiting a tendency to spontaneous cure. Probably in 20 per cent. of cases the disease is amenable to treatment other than operative. In what does the non-operative treatment consist? First, in the removal of all predisposing causes, such as malaria, anæmia, exhaustion, or any peripheral irritation, such as a carious tooth or antral disease; secondly, in the administration of drugs, and the drug which is *par excellence* the most efficacious, especially so in the exhausted and anæmic, is strychnine. In cases of but one or two years' standing, strychnine properly administered will arrest or control the disease almost invariably; but in order to obtain this result the drug must be administered in heroic doses, and the patient must be kept under the closest observation, and should be confined to bed. The remedy is administered hypodermically once daily, in gradually ascending doses, until, at the expiration of two weeks, the physiological limit is reached. Thus, beginning with one-thirtieth grain daily, the dose may be increased to one-tenth or one-eighth or higher, and when the maximum dose is reached it should not be given oftener than once on alternate days. After the pain has entirely disappeared the drug should be gradually withdrawn. As adjuvants to this treatment rest is regarded as of the utmost importance, and iodide of potash and the tincture of the chloride of iron as more or less helpful. One of the patients which you have seen to-day had enjoyed relief, only

temporary, however, from this mode of treatment. The symptoms recurred and a radical operation was performed.

Depending, as I have said, upon the duration of the disease and the severity and frequency of the attacks, it is perfectly proper and justifiable, for a period not exceeding a year at the utmost, to give medicinal measures a fair trial. If, however, at the expiration of this time or sooner, if the attacks are very frequent and severe and uncontrollable, every means of combating the attack have proven partially or altogether futile, it is your duty to recommend to your patient operative intervention as the only hope of relief.

This carries us up to the consideration of the operative treatment of trifacial neuralgia, and before discussing the respective operations let me tell you that all operative procedures for the relief of tic douloureux may be divided into two classes, according to whether the seat of operation is extracranial, *i. e.*, peripheral, or intracranial, *i. e.*, central.

What are the indications for each of these classes? If the physician was but able to distinguish between those cases in which the lesion was in the ganglion and those which were not, this perplexity would not exist; the indication for the peripheral or intracranial operation would be clearly defined; but, unfortunately, no means as yet have been suggested by which such a differential diagnosis may be established. Other considerations, therefore, must guide us in the selection of one or the other of these operative procedures, and chief among these is the number of branches involved. We ask the question—Is the pain confined (1) to one branch of one division, as the infraorbital branch of the second division, or the inferior dental branch of the third division; or (2) is the pain referred to all the branches of one of the three divisions; or (3) is the pain referred to the distribution of more than one division (if two it is usually the second and third divisions), or to all three divisions of the trigeminus?

The operations which may be required to meet one or the other of these indications are neurectomy (the so-called peripheral or extracranial operation), division of the second and third divisions at their entrance to the foramina and interposition of rubber tissue, extirpation of the ganglion and division of the sensory root (the so-called central or intracranial operations).

If, as so often happens in the early history of these cases, the pain is restricted to either the distribution of the inferior dental or the infraorbital branch, there is no question but that a peripheral or extracranial operation is the operation of choice, and for the following reasons: first, because in a certain percentage of cases it will be followed by absolute recovery; second, because in a still larger percentage it will be followed at least by a remission for varying periods of time; and third, because it is unattended with the risks that accompany the

intracranial operation. In order to ensure the best results these operations should consist in a resection not of a small section, but of such an extensive section of the nerve as would make regeneration highly improbable. In the case of the inferior dental all that portion of the nerve between the inferior dental foramen and the mental foramen should be resected. In the case of the infraorbital nerve, that portion between the foramen rotundum and the infraorbital foramen should be resected. When a peripheral operation has not been carried out as thoroughly as it should have been, the pain will recur almost invariably, because the defect in the nerve has been repaired. In exceptional cases, even when a very extensive resection has been performed, as, for example, when the inferior dental nerve has been removed intact in its entirety from the dental to the mental foramen, that whole section of the nerve has been regenerated.

In order to guard against this the orifices of the dental canal should be plugged with some substance which the nerve fibres cannot penetrate. I have used silver foil in several cases, and up to this time with satisfactory results.

When recurrence follows one or more peripheral operations, or when the distribution of the pain becomes more widespread and is no longer limited to one but is referred to two or all the branches of the trigeminus, the period in which the peripheral operation is indicated has passed. There remains to be considered one or the other of the intracranial or central operations, and, of these, the two which are deserving of the most consideration are the division of the sensory root and the division of the second and third divisions at their entrance to their respective foramina.

The technique of operations upon the Gasserian ganglion has been so improved in recent years that they no longer belong to the "kill or cure" class. As a result of a careful study of the anatomical relations of the ganglion and of a better method of exposure, the mortality of these operations has been very materially reduced. While operations which have for their object the extirpation of the ganglion have been practised for a number of years, the recently suggested operation, that of dividing the sensory root, possesses many advantages. Chief among these are: (1) that it should be attended with a lower mortality; (2) that it obviates a number of difficulties; (3) that its execution is, comparatively speaking, simple; and (4) that the integrity of adjacent structures, more particularly the cavernous sinus and sixth nerve, are not endangered. This operation is practically complete when the posterior aspect of the ganglion and its sensory root have been exposed; that is, it is practically completed before one encounters the serious and troublesome difficulties experienced in attempts to extract the ganglion. Apart from these advantages, this procedure would seem to have special

indication in those cases in which there was special reason for believing that the lesion was in the ganglion itself; by severing the connection between the ganglion and the central nervous system, the division of the sensory root is a positive guarantee against the recurrence of pain. The success of this operation depends upon the inability of the sensory root to undergo regeneration, and only after having proved this could one render an absolutely favorable prognosis. Before introducing this operation, which was suggested by my colleague, Dr. Spiller, to the profession, a very thorough and painstaking investigation as to the possibility of regeneration was conducted on the lower animals. The operation, as now practised on the human subject, was repeated by Dr. Spiller and myself upon dogs; the specimens removed after varying intervals subsequent to the operation failed to show the least sign of nerve regeneration. As yet, it has to be proven that regeneration of the central nervous system ever occurs.

The method of performing this operation does not differ materially in its early steps from the operation having for its object the removal of the ganglion. The so-called Hartley-Krause or temporal route is chosen; a horseshoe-shaped musculocutaneous flap is reflected, the zygoma is chiselled through at either extremity in order to obtain freer access to the ganglion, a section of the skull measuring 3 to 4 cm. is removed with gouge and rongeur forceps. Up to this point the operator has no special difficulties with which to contend, but from now on he will be engaged in one of the most difficult operations upon the human subject, and one requiring the maximum of patience. The operator now proceeds to separate the dura from the base of the skull until one of three landmarks appears—the foramen spinosum, from which emerges the middle meningeal artery, which must be carefully avoided or deliberately ligated; the foramen ovale, through which the third branch makes its exit, and the foramen rotundum, through which the second division finds its way out of the skull. These landmarks will usually appear in the order named. While this step of the operation is in process of execution, hemorrhage of varying degrees, but always severe enough to be most troublesome, though never alarming, is the great bugbear. Controllable only by pressure, one must expect to pause many periods of from one to five minutes in order to control the bleeding sufficiently to enable one to recognize the structures. When the margins of the foramen rotundum and ovale are fully exposed, the operator then proceeds to the next step necessary for the exposure of the ganglion, and reflects a flap of the dura propria. This is best accomplished by making an incision through the dura propria between these two foramina, and separating the dura only from the upper surface of the ganglion. It is not necessary to disturb the lower surface of the ganglion in the operation we are describing, and this is fortunate,

because from this surface the ganglion receives most of its blood supply. The dura is to be separated then only from the upper and posterior surface until the sensory root is exposed. Pick the sensory root up on a short blunt hook and remove a small section of the nerve with blunt, curved scissors. With the completion of this step the operation is practically finished. One or two strands of gauze are introduced to afford proper drainage, and the musculocutaneous flap replaced and sutured. I exhibit before you to-day three patients upon whom I have performed this operation as above described. This patient was operated upon over a year ago, and was the first patient upon whom this operation was ever practised. That he has remained entirely free from recurrence is the strongest possible evidence that could be advanced in confirmation of the statement which we have made regarding regeneration of the sensory root. The patient now before you is the second case of the series. She was operated upon a few months ago; her convalescence was uninterrupted, and she has continued absolutely free from pain. After the hair grows in, there will be scarcely any disfigurement apparent. The third case was operated upon about five days ago before a limited section of the class. She likewise has given us no cause for alarm. When I remove the dressing you will see the two drainage strips of gauze emerging from either angle of the wound. These I usually leave *in situ* for from three to five days, since the oozing usually continues for this period of time. The stitches are removed on the sixth day, and on the day following the patient may get up out of bed, and at the expiration of two weeks may leave the hospital.

For the reasons already stated I am inclined to believe that this operation will in time replace the extirpation of the ganglion. Abbe, of New York, has performed an operation which is less radical and less difficult, but its field of usefulness is limited to these cases in which only the second and third divisions are involved. It, likewise, is an intracranial operation, and consists essentially in the division of the second and third divisions where they are given off from the ganglion, and in the interposition of rubber tissue at the point of division, in order to prevent the severed nerves reuniting with the ganglion.

In the future I should be strongly inclined to practise temporary closure of one common carotid artery as a means of controlling hemorrhage during the exposure of the ganglion. If, as it is claimed, this preliminary procedure can be carried out without endangering the patient's life or permanently impairing the function of the brain, it will prove to be one of the most important contributions to the technique of these intracranial procedures. Not only will the amount of hemorrhage be very materially reduced, but the time required to complete the operation will be lessened by at least one-half. I have practised temporary closure of the common carotid arteries with the most gratifying results

in a number of operations—*e. g.*, in the removal of a brain tumor, in the excision of superior maxilla and excision of the tongue—and I see no reason why this blood-saving and time-saving measure should not be taken advantage of in operations upon the ganglion.

1. To sum up in a few words the treatment of trifacial neuralgia I would say that in all incipient cases remove the predisposing cause and administer strychnine hypodermically in heroic doses under proper precautions, and with such adjuvants as have been suggested.

2. In cases that do not respond to this mode of treatment, where the pain is referred to but one branch, recommend the peripheral operation, even though the operation may have to be repeated. It will afford relief, at least temporarily, in every case, and in some cases permanently.

3. When the peripheral operation has failed to afford but temporary relief, even though it may have been properly executed and repeatedly performed, or when from the onset the pain is referred to two or more branches, recourse should be had at once to an intracranial operation: either division of the sensory root or, in certain selected cases, division of the second and third divisions, with interposition of a foreign substance to prevent reunion.

A DEATH DURING GENERAL ANÆSTHESIA WITH ETHYL CHLORIDE.

By Francis Olcott Allen, Jr., M.D.,
of Philadelphia.

On August 11, 1903, there was admitted to the Pennsylvania Hospital a colored man, I. W., aged twenty-eight years, suffering from an incarcerated inguinal hernia. The patient was an epileptic and had had his last convulsion three days before admission. He had had the hernia for three years; it had been easily reducible until ten hours before admission. Since that time he had had pain in the hernia and considerable vomiting, not, however, fecal in character.

Physical examination showed his abdomen greatly distended and tympanitic, and a large, irreducible scrotal hernia on the right side. Temperature was 98.8° F.; pulse small, 110 per minute. Examination was otherwise negative. His general condition was poor.

The hernia could not be reduced, and he was prepared for operation.

Anæsthesia was started with ethyl chloride and progressed satisfactorily until narcosis was approaching (about three or four minutes), when the change to ether was to be made. About fifteen grams of ethyl chloride were used. Just as ether was started the patient gagged and vomited an enormous quantity of an almost clear, watery liquid, which, for a time, spouted from his mouth in a continuous stream, without retching or inspiratory effort. The vomiting could not be controlled and must have lasted, with slight intermissions, for two or three minutes.

When it finally stopped respiration was not resumed, cyanosis was present, and no pulse could be felt. Artificial respiration, with traction on the tongue, was continued for some minutes without effect; there seemed to be no air entering or leaving the lungs. No obstruction could be felt in the throat or trachea. There had been no solid matter in the vomitus. Permission for an autopsy was refused by the patient's friends.

During the last six months ethyl chloride has been used at the Pennsylvania Hospital quite indiscriminately for inducing general anæsthesia for minor operations or as an antecedent to ether for more prolonged narcosis. The results have been generally satisfactory. In some cases there has been struggling; in one child an epileptiform convulsion occurred during the induction of anæsthesia; in no case, except the one above reported, have there been alarming cardiac or respiratory symptoms. The method has been to spray the chloride of ethyl upon gauze held over the patient's nose and mouth, and the number of such anæsthetizations has been about one hundred.

This case is not reported to condemn ethyl chloride or emphasize its dangers, for it can hardly be held entirely responsible for the fatality; the result might have been the same with any other anæsthetic. The statistics of general anæsthesia with ethyl chloride are given in the *Journal of the American Medical Association* for November 8, 1902, by Dr. M. W. Ware, who collected 12,436 cases with one *bona fide* death; and in the *Lancet* for April 4, 1903, by Dr. W. J. McCardie, who mentions 16,000 cases, collected by Seitz, with one death.

A CASE OF INFECTION OF THE EPIDIDYMIS AND TUNICA VAGINALIS BY THE FRIEDLÄNDER BACILLUS.

By Eugene P. Bernstein, M.D.,
ASSISTANT IN THE PATHOLOGICAL LABORATORY OF THE MOUNT SINAI HOSPITAL, NEW YORK CITY.

Although the literature abounds in observations of infections by the Friedländer bacillus, the number of cases arising in the genito-urinary tract is very small. The occurrence of the organism in the respiratory tract, as a causative factor in pneumonia, pleurisy, and empyema is well known, and its etiological sigificance in certain cases of otitis media, meningitis, cholecystitis, and intestinal infection has been established.

Etienne, in an exhaustive article comprising eighty-three cases collected from the literature, describes instances of primary infection in almost every organ of the body. In the genito-urinary tract he describes lesions secondary to a septicæmia.

In the cases reported by Canon, Clairmont, Brunner, Weichselbaum, Howard, and Josserand and Bonnet, the Friedländer bacillus was isolated from the kidneys and in two cases from the urine; but these cases were not instances of primary infection.

Moutt-Saaverdo gives a short account of two cases of cystitis, and Shenk describes a case of bilateral salpingo-oöphoritis due to the bacillus.

Of more interest are the cases of Halban, Malgaigne and Vauverts, and Chiari. In Halban's case a scrotal hæmatocele became infected and from the pus the Friedländer bacillus was obtained in pure culture. The mode of infection could not be ascertained. Malgaigne and Vauverts found the same organism in both spermatic cords and the urethra in an infection subsequent to an acute specific urethritis. In Chiari's case some doubt exists as to the primary seat of infection. He concludes from a study of his case that the cystitis was the cause of an ascending suppurative pyelonephritis followed by a fatal septicæmia.

When we consider that these few observations represent all that has hitherto been seen in the way of infections of the genito-urinary tract by the Friedländer bacillus, the following case becomes one of decided interest.

History (abstract). The patient, a male, aged fifty-eight years, was admitted into the Mount Sinai Hospital on July 6, 1902, under the care of Dr. A. A. Berg, to whose kindness I am indebted for the clinical history.

Family History. Negative.

Previous History. Gonorrhœa at the age of twenty-two years and pneumonia at the age of fifty-one years.

The present history is of three weeks' duration. At that time his right testicle suddenly became swollen, red, and tender. One week later the left testicle was similarly affected, while the inflammation of the right diminished somewhat in severity. He claims to have had no chills or fever. Urination and sexual power normal. There are no other facts of importance.

Physical Examination. The right testicle is hard, and swollen to about one and a half times its normal size; it is not very tender, nor is there any fluctuation present. The right spermatic cord is distinctly thickened. The left testicle is of the size of a large orange and is very tender. The skin over it is glossy and reddened. The consistence of the tumor mass is hard, except at the lower anterior portion, where fluctuation can be felt distinctly. The left spermatic cord is of the thickness of the index finger. There is no urethral discharge. Rectal examination reveals nothing but a slight prostatic hypertrophy. On massaging the seminal vesicles a few drops of purulent-looking secretion appear at the meatus. On examination gonococci are not present.

The operation, which consisted of incision and drainage of the left tunica vaginalis, revealed the following conditions: The tunica vaginalis is much thickened and filled with a very viscid, yellowish pus.

The epididymis is the site of numerous small abscesses. The testicle appears to be normal. Spreads from the pus show a Gram negative, encapsulated bacillus. The cultures will be described later.

Five days after the operation the right testicle began to increase in size, became tender, and showed distinct fluctuation. The seminal vesicles also became much indurated and tender. Aspiration of the right tunica vaginalis yielded the same viscid, yellowish pus.

At the second operation the right tunica vaginalis was incised and drained. A large pelvic abscess was found on the left side. This was evacuated by an incision just above the left Poupart ligament, and a counter-incision was made in the perineum. About fourteen ounces of non-odorous, yellowish pus was evacuated. The left spermatic cord was also incised, and pus, similar to that previously described, was obtained.

It is unnecessary to go into the further clinical history of the case except to state that the patient made an uneventful recovery.

The urine, which contained many pus cells and a few granular casts, was not examined bacteriologically. The finding of the Friedländer bacillus in it would not have been of much significance, as it might have been infected from the epididymis.

Bacteriological Examination. The findings in the pus obtained at the different operations are all identical. The organism is a non-motile, facultative anaërobe. Spores and flagella cannot be demonstrated.

The spreads show a rather short, plump, Gram negative bacillus with rounded ends, surrounded by a broad capsule, which is well demonstrated by the ordinary methods for staining capsules (Welch and Weichselbaum) and by the writer's modified Gram stain, which is very well adapted for the demonstration of capsules.[1] There is a tendency here and there for the organism to grow in short chains. There is no decided variation in the size of the organisms.

Agar Plates. Macroscopically the superficial colonies are more or less rounded in shape, well elevated above the surface, and show a sharply defined edge. They are rather grayish-white in color, mucoid in appearance, the surface being glossy. The deeper colonies are small, round or oval, pale yellow or yellowish-gray in color.

On microscopic examination the superficial colonies are of a yellowish-gray color, almost opaque in the centre, and more transparent toward the periphery. The edge is regular and well defined, and the colony as a whole is of a homogeneous structure. The deep colonies are round or oval, of a deep-brown color, with a distinct edge. The colony is finely granular and quite opaque.

Surface inoculations on agar show considerable growth in the form of rather diffuse mucoid colonies, which adhere rather tenaciously to each other, being drawn into long threads when an attempt is made to remove some of the colonies with a platinum loop.

Stick cultures in agar show the growth along the entire puncture, with a diffuse, thick growth over the surface.

[1] The writer's method is as follows: After fixing the specimen, it is stained with anilin-water-gentian-violet for thirty seconds; the Gram solution is then used for twenty seconds; alcohol until complete decolorization ensues. The specimen is washed in water, and is then counter-stained for thirty seconds with a 12 per cent. aqueous solution of fuchsin (made from a saturated alcoholic solution).

Gelatin Stick Cultures. Growth along the entire puncture, and diffuse growth on the surface; no gas formation or liquefaction of medium.

Bouillon. Diffuse marked cloudiness, with slight sediment at the bottom of the tube. Considerable scum on the surface.

Glucose-agar Stick Cultures. Numerous gas bubbles within six hours.

Glucose-bouillon (0.5 per cent.) and *Saccharose-bouillon* (0.5 per cent.). Diffuse cloudiness; slight sediment; no scum formation; distinct acid production in twelve hours. *Lactose-bouillon* (0.5 per cent.). Growth less marked.

Fermentation Tubes. Glucose-bouillon. Growth in the branch and in the bulb; acid production marked; gas formation.

Saccharose-bouillon. Growth in the branch and bulb; very marked acid production; more than twice as much gas formation as in the glucose medium.

Lactose-bouillon. No growth in the branch; slight growth in the bulb with alkalinity production.

(All stock bouillon sugar-free. Glucose, saccharose, and lactose media contain 0.5 per cent. of the respective sugars.)

Milk. Distinct acid production; no coagulation, even after thirty days.

Indol. Moderate reaction on the fourth, fifth, sixth, and seventh days; more marked on the eighth day.

Potato. Heavy, prominent, yellowish-gray mucoid growth; gas bubbles on the surface.

Serum-agar. Very marked growth; more abundant than with ordinary agar. No precipitation; no gas formation.

On the *sugar-serum-agars* (devised by Libman) there is a very heavy growth. Precipitation on the glucose and saccharose media with gas production, but none on the lactose medium.

Serum Reactions. The patient's blood gave no reaction with the organism, either in the form of threads or of clumps, when tested in weak and strong dilutions.

Animal Experiments. Intravenous and intraperitoneal inoculations into rabbits were without apparent effect. Guinea-pigs invariably succumbed within twenty-four hours after intraperitoneal injection, and a very marked general peritonitis, from which the organism was recovered, was always found.

It is evident, from the description which precedes, that the organism found in our case is a typical Friedländer bacillus. It is of interest to note that the organism is more active in splitting up saccharose than it is in splitting up glucose, and that lactose is not at all affected. It has been our experience in the laboratory that this property is quite characteristic of a number of members of the Friedländer group. The presence of a positive indol reaction is in accord with the work of the later investigators. The absence of agglutination or thread formation in the serum test is a rather striking phenomenon in so marked an infection. The point of invasion of the organism remained undiscovered. The moderate severity of the case clinically was in striking contrast to the severity of the infectious process.

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A CASE OF THE EPIPHENOMENA OF DIPHTHERIA ANTITOXIN.

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IT has come to pass that in the ordinary practice of medicine the giving of an injection of antitoxin in a case of diphtheria is regarded as about devoid of all danger. It is true that most of us have occasionally seen a mild urticaria—coming on about forty-eight hours after injection—follow the use of the medicament. A still smaller number of practitioners have seen joint stiffness, endocardial murmurs, and atypical symptoms of acute rheumatism develop anywhere from seven to fourteen days after injection. A few will remember, in a hazy way, of a few cases having been reported in the early days of antitoxin, wherein the reporters attributed the rapid and sudden death of their patients to the antitoxin; but so many times has the remedy been used without mishap that these cases have come to be looked upon as coincidences.

It is, therefore, my purpose in placing the following case on record to call the attention of the profession to the fact that the injection of antitoxin is once in a great while followed by alarming symptoms. It is not to be a doubt cast upon the efficacy and great value of antitoxin, which has now been abundantly proven, but a protest against looking upon an injection of antitoxin in the same light as a hypodermic injection:

On December 14, 1902, Miss W., aged thirty-nine years, and a matron by occupation, noticed that her throat was sore. This condition continued, gradually increasing in severity, until the 18th, when she went to bed, and I was called to see her. A clinical diagnosis of diphtheria was easily arrived at, and arrangements were made to give an injection of antitoxin on the 19th.

There was nothing in the family or personal history of the patient which is worthy of mention.

At about 11.30 A.M. of December 19th I injected into the subcutaneous tissue of the back of this patient the contents of a bottle labelled: "N. Y. State Department of Health. Diphtheria Antitoxin. 1500 units of Antitoxin, op. No. 1111 A 7. An '02,'" and immediately took my departure.

About ten minutes after receiving said injection the patient was taken suddenly with a feeling like sulphur fumes in the bronchial tubes, and could not breathe. She is said to have at once become very much cyanosed and semicomatose, and, in fact, her attendant thought that she was in *articulo mortis*. The patient says that at this time she felt a "numb" feeling extend over her body and that she could not see anything in the room. Next there developed a severe pain in the epigastric region, and the patient vomited, and immediately thereafter a severe itching, stinging rash came out all over the body. As the rash appeared the other symptoms passed away, and the whole process had lasted up to this time about fifteen minutes.

I reached the bedside of the patient about one and one-half hours after the injection of antitoxin had been administered, and found her suffering from a universal urticarial rash, the conjunctivæ excessively swollen and injected, so much so as to interfere markedly with the action of the lids.

It took about thirty-six hours for this rash to entirely disappear, and the patient's convalescence was very rapid and uneventful. The action upon the tonsillar membrane was very marked and energetic, the whole having disappeared in twenty-four hours.

When questioned this patient told me that she had always noticed that while driving behind a horse her eyes would run and that she would be affected by uncontrollable sneezing attacks, and that when she was a young woman she repeatedly had to desist from harnessing her horse because of these attacks.

From a careful questioning of the attendants on this patient I am convinced that this case came very nearly being fatal, and had the dose been larger death would have certainly occurred.

I am equally clear that the symptoms are not due to the antitoxin *per se*, but to an idiosyncrasy on the part of this patient to contact with a horse or anything derived from that animal.

A CASE OF PROBABLE PRIMARY CARCINOMA OF THE LUNG.

By Arthur Bremken, M.D.,
of Spring Grove, Ill.

While in the service of Dr. Bayard Holmes he placed before me the following history of a case which he had seen with Dr. I. C. Anker and Dr. Robert H. Babcock:

Mrs. B., aged fifty years, came under the care of Dr. Anker on November 30, 1901. She had been previously under the care of another physician, complaining of pain in the left chest, and this physi-

cian had repeatedly made physical examinations of the chest and had assured her that there was nothing wrong with the lungs or heart. She still felt this pain for which she had consulted the first physician, and it was sharp enough to give rise to uneasiness in her mind, but gave her no pain or anxiety between the attacks of coughing.

Dr. Anker found a woman, aged fifty years, mother of several children. She had ceased to menstruate ten years ago. She had had no discharge from the uterus and had considered herself during all this time a well woman. She weighed 120 pounds, had brown hair with very little gray, and was in every way a well-preserved woman. Upon the first examination Dr. Anker detected an area of relative dulness in the lower part of the region of the left lung. He suspected tuberculosis and attempted to get an examination of sputum, but she had none. He saw her repeatedly during the following three months, during which time the patient continued to use acetanilid in five-grain doses, three or four times a day, to relieve the attacks of pain which she continued to suffer. During the last of January, 1902, the whole lower half of the left lung seemed to be flat, and the heart seemed to be pressed toward the right. Early in March Dr. Robert Babcock saw her in consultation with Dr. Anker, and found all the physical signs and conditions which Dr. Anker had recognized. He believed that the lung was surrounded by a solid, fibrinous effusion, and that the heart was so displaced that the apex was almost exactly in the middle line. Upon a second visit to her Dr. Babcock suggested the possibility of some fluid exudate at the base of the left lung. On account of his inability to make a diagnosis he recommended that aspiration be undertaken. During all of the time the patient had been under the care of Dr. Anker she never had a temperature above 100° F., and only occasionally a pulse below 100; the pulse ranged between 100 and 110. The urine was repeatedly examined and gave no evidence of abnormal constituents, except in the three or four weeks previous to my visit there was a distinct increase of bile pigment. During the last three weeks the stools were found to be white or clay-colored and free from bile, and in the last four months she has been persistently constipated, and during the last three weeks she has been obliged to have a little heroin to relieve the cough which has troubled her. For three weeks she has complained of indistinct abdominal disturbance and distress in the upper part of the abdomen. This pain was relieved by pressure of her hands or arm. On March 19th I saw her with Dr. Anker and Dr. Kitterman. It was in daylight, and she gave the impression of a woman who had been moderately sick. She was somewhat thin, weighing about 112 pounds. Her complexion was not good, but was not cachectic, and there was a slight trace of jaundice in the conjunctiva. She was suffering from dyspnœa and could only speak in short sentences, broken by rapid breathing. Her lips were blue, but there was a distinct flush on her cheeks. Her pulse was 120 when first taken. She had just had a dose of acetanilid. The pulse presented no unusual character and was found to be approximately the same at both wrists. After removal of the clothing her chest showed a distinct bulging toward the left side. The heart's apex was readily recognized at about the midsternal line. There was distinct curvature of the spine, apparently due to the distention of the left chest. The liver was readily recognized, extending two finger-breadths below the costal arch. The

abdominal muscles were fixed and rigid. The area of tympany of the stomach was 1.5 inches above the umbilicus and certainly not greater than normal. The upper part of the area of the left lung from the apex to the attachment of the diaphragm below was absolutely flat except for an inner strip near the vertebræ behind and the sternum in front. This area was also devoid of respiratory sounds and without fremitus or vocal transmission. The inner margin next to the sternum and vertebræ gave slight respiratory sounds and slight vocal transmission, but no fremitus could be felt. Percussion and auscultation of the right chest were practically normal, or if abnormal they were puerile or exaggerated. The area of cardiac dulness extended two and a half inches beyond the middle line toward the right and upward for a distance of three inches.

The patient's temperature at this time was 99° F. and had been 99.5° F. in the morning. Her urine had been examined this day, giving no abnormal constituents except an unusually large amount of bile. She had slept moderately well during the night. Her bowels were moved by saline cathartics; the stools were clay-colored. She had no difficulty in swallowing, but was obliged to eat slowly on account of the dyspnœa.

On withdrawing a drop of blood for examination, it appeared to be very dark colored and venous. It flowed readily enough. The count gave 15,000 leucocytes per c.mm. No red count was made nor was hæmoglobin estimated.

After removing a local application from the left side of the chest the skin was scrubbed and local anæsthesia produced by injecting a dilute solution of cocaine into the skin and deep tissues of the chest wall. A trocar about 1 mm. in diameter was introduced between the fourth and fifth ribs in the axillary line. Before the trocar was removed a bloody serum began to pour out between it and the cannula. After withdrawing the trocar eight ounces of fluid were collected in a clean glass for examination, and afterward thirty-two ounces were allowed to run out in an intermittent stream after contraction of the abdomen and upward compression of the diaphragm. The patient was in a sitting position during this operation. After the stream began to flow more slowly the cannula was removed for fear of introducing infection. The patient immediately improved in voice and respiration after this fluid had been removed. The heart was found to have moved at least one inch toward the left, but there seemed to be no increase in resonance over the left lung. The apex was especially flat.

Three weeks later the dyspnœa had returned and the Bunsen pump was used to empty the left thorax again; but, naturally, the amount of fluid removed could not be determined. When the vacuum became considerable the patient complained so much of pain and cardiac distress that the operation was arrested. The findings were the same as before. Examination of the fluid showed: specific gravity, 1025; reaction alkaline; urea, 0.2 per cent.; a large amount of albumin, a few leukocytes, mostly lymphocytes, and erythrocytes 8400 per c.mm. After this no further attempt was made to secure expansion of the lung. The patient died August 31st, and the autopsy was made by Dr. Anker:

Left pleural cavity contained about three pints of thick, bloody fluid of a brownish-red color. No adhesions were present. The left lung was about the size of two hen's eggs. The upper portion or lobe was

very friable and bloody; the lower portion was rather hard to the touch and contained considerable blood. The parietal pleura was smooth and glistening. No enlarged lymph glands were found in the mediastinum.

The parietal and visceral pleuræ of the right pleural cavity were smooth and glistening. There were no adhesions. No enlarged lymph glands were found. The lung was about one-third the normal size. Small white miliary nodules were seen in the visceral pleura.

The apex of the heart was in the sternal line. There were no adhesions. No further notations were made.

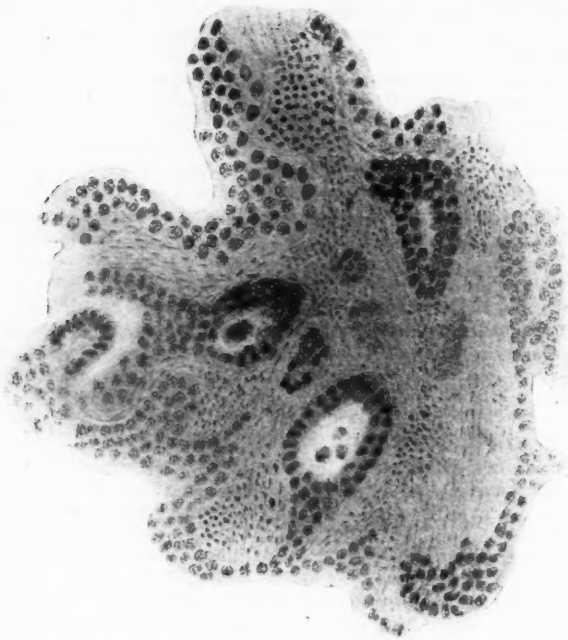
The aorta was bound to the surrounding structures, particularly to the posterior wall of the thorax, and appeared to be atheromatous.

The diaphragm was thickened throughout, but more particularly on the left side, and it could plainly be seen that the thickening was due to the neoplastic invasion. The aorta, diaphragm, and heart were bound together apparently by the tissue that caused the thickening of the diaphragm. No adhesions were found in the peritoneal cavity. The peritoneum was smooth and glistening and no fluid was found in the peritoneal cavity. The omentum was uniformly thickened, somewhat nodular, and showed small areas of fat. The liver was apparently normal in size and outline. The gall-bladder presented no adhesions. It was greatly distended with a translucent material. Its walls appeared slightly thickened. There were no adhesions about the stomach, no tumor in the pylorus, and no enlarged lymph glands about it. The intestines, spleen, pancreas, and kidneys were examined and showed no apparent anatomical changes.

I made the pathological studies which follow and such drawings as illustrate the findings in a large series of sections stained by various methods:

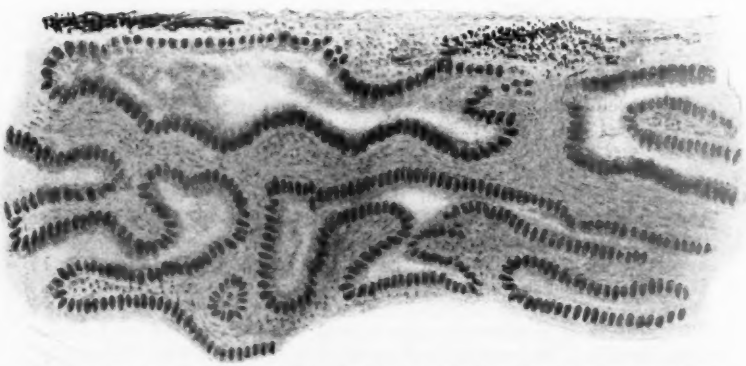
A section from an area of consolidation including the margin of the lung shows irregular islands of epithelial cells. These cells are separated from each other by a connective-tissue stroma, rich in well-staining connective-tissue nuclei. Finger-like projections of the stroma are seen everywhere. The arrangement of the cells in the groups is always more or less characteristic. The outer layer of cells or those in contact with the stroma are cylindrical, while the others or those lying internal to this layer are more or less irregular in outline, and they vary in size. As we reach the periphery of the tumor an entirely different picture presents itself. Here it attains the type of a cystoadenocarcinoma (Figs. 1 and 2). The cyst-like spaces here are lined with a single layer of columnar epithelium. An amorphous eosin staining material fills these spaces, in the meshes of which roundish cells are occasionally seen, about the size of large lymphocytes. These stain faintly with hæmatoxylin. This amorphous material is seen now and then in the large masses of epithelium in the deeper parts of the tumor (Fig. 1). The nuclei of the tumor cells vary somewhat in size and shape. They usually stain well with hæmatoxylin and show nucleoli. Degenerative changes in these cells occasionally appear, especially in the large masses of epithelium. Karyokinetic figures are met with. The bloodvessels in this area show proliferative changes in the intima, apparently endarteritis obliterans, in many cases occluding the lumina. Black pigment

FIG. 1.



Drawing from tumor in left lung, from the most solidified portion, showing the characteristics of carcinoma. Oc. 4, obj. 7, Leitz.

FIG. 2.



Drawing from a section of tumor in left lung at its pleural periphera, showing cystoadenocarcinoma. Oc. 4, obj. 7, Leitz.

is sometimes found in the stroma, and is deposited in moderate amount around the bloodvessels. Small round-cell infiltration is found everywhere.

A section of lung in the vicinity of diffuse consolidation shows in a general way the same findings—adenocarcinoma. In this region the alveoli are in many places filled with cylindrical epithelial cells. A single layer of tumor cells lines the alveolar wall. Many transverse sections of bloodvessels are met with; they are mostly empty. Around many of them (especially around the larger ones) the invasion of the tumor

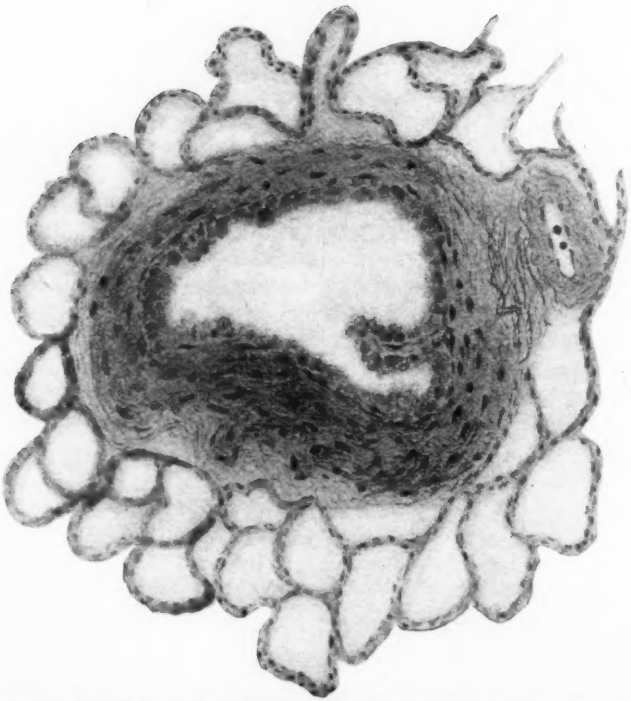
FIG. 3.

Drawing from solidified area of left lung, showing irregular channel, which in all probability is a bronchus, containing finger-like projections of epithelium. Oc. 4, obj. 3, Leitz.

cells into the adventitia is to be seen. Small bronchi are observed; their lining epithelium is usually intact. Peribronchial round-cell infiltration, which many times extends through the entire wall of the bronchus and impinges on the lumen displacing the epithelium, is often recognized. Lying in the meshes of the invaded lung, surrounded with the tumor cells, is to be seen an irregularly outlined channel, appearing as though it were compressed by the surrounding mass. In the wall of this channel are rather oblong nuclei, which stain fairly well with hæmatoxylin and appear to be granular. From their size and general appearance one would say they were muscle nuclei, and would come to

the conclusion that the channel was a bronchus. Within the lumen we see epithelial cells, which are more or less cylindrical and simulate those normally found lining a bronchus. There is more than one layer of these cells in places. Extending into the lumen of this channel one sees what appears to be a proliferation of these cells into finger-like projections. In one corner a mass of these lie, seemingly unattached to the wall (Fig. 3). A channel corresponding in its histological appearance to the one above described is seen in a part of the lung

FIG. 4.



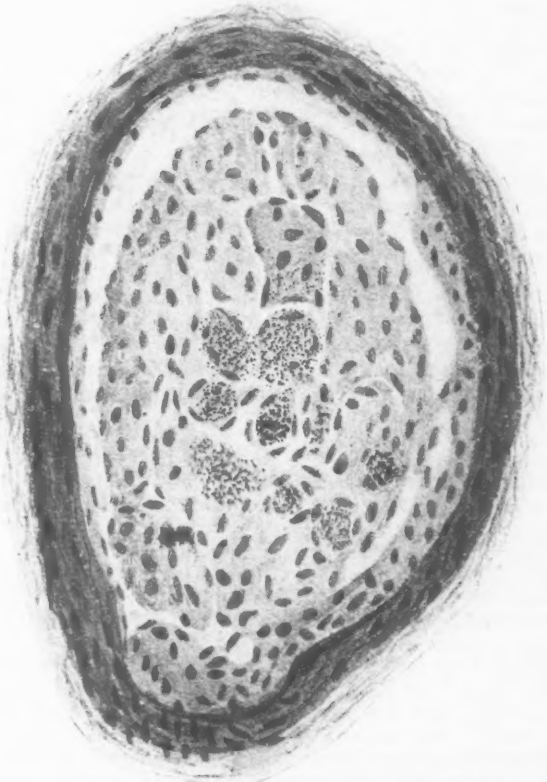
Drawing from left lung remote from diffuse infiltration, showing transverse section of bronchus with a papillary node projecting into its lumen. Oc. 4, obj. 7, Leitz.

remote from the diffuse infiltration. It is irregular in outline and lies beside a bloodvessel. It is probably a bronchus. A distinct papillary node, lined with cylindrical cells, is seen projecting into the lumen. A direct connection with the wall is demonstrable (Fig. 4).

A section of lung remote from consolidation shows a tendency to peripheral distribution of metastases. It shows also how the alveoli are invaded, some being only partially filled, while others are filled to distention. Those alveoli that are not invaded by the tumor cells are usually markedly distended, giving the picture that is seen in emphysema.

Throughout this area is seen desquamation of the alveolar epithelium. These desquamated cells are always filled with a brown pigment. Lymph spaces in the alveolar septa and subpleural lymph spaces are occasionally distended with lymphocytes and black pigment. The blood-vessels in this section are always filled with blood. The picture of endarteritis is present in many of them.

FIG. 5.



Drawing from bloodvessel in right lung, showing proliferation of endothelium in a tumor-like manner, simulating the picture of endothelioma. Oc. 4, Leitz.

A section from the right lung shows peripheral metastases into the alveoli. The cells usually form but a single layer around the alveolar wall. Small areas of pneumonia are occasionally seen in the right lung. Pigmented desquamated alveolar cells are found throughout. The blood-vessels are always engorged with blood. Here, as in the left lung, endarteritis obliterans is present. Nodes of proliferated endothelium extend into the lumen and divide the vessel into two channels. Near the margin

of the lung is seen a relatively large bloodvessel, with a rather thin wall for so large a lumen (Fig. 5). The entire vessel is filled with a tumor-like mass apparently springing from its endothelial lining. It is attached at the lower margin. The endothelial cells that have proliferated have produced the picture of an endothelioma. Brownish pigment is present in the central portion, illustrating beautifully complete organization of a thrombus. Perivascular lymph spaces in this section are occasionally filled with the tumor cells.

The tumor in the omentum attains throughout more the type of a cystoadenocarcinoma. The cyst-like spaces are larger, some being entirely empty, while others are filled with an amorphous eosin staining material. The stroma is here composed of a more delicate framework, and gives the general appearance of lymphadenoid structure. In many places small distinct openings are seen always lined with endothelial cells. Some of these openings are filled with lymphocytes, others are empty, and many are filled with tumor cells. The stroma is densely infiltrated with lymphocytes. Here and there are small areas of fat cells, around which there is always a dense leukocytic infiltration. Between the fat cells there are rows of infiltrating tumor cells. The bloodvessels here usually have thin walls and otherwise appear normal. They do not show the changes observed in the bloodvessels of the lungs. They are usually distended with red blood corpuscles, but no thrombus formation. Perivascular leucocytic infiltration is everywhere to be seen.

A section through the thickened diaphragm shows that the thickening is entirely due to the neoplastic invasion. The tumor is seen at one point penetrating the muscular tissue from one surface to the other—adenocarcinoma displacing the muscle fibres. Isolated muscle fibres are present in the new-growth. In its progress through the diaphragm the tumor has produced a pressure atrophy of the muscle fibres. Many fibres are less than one-third their normal size. Leukocytic infiltration is present in a moderate amount throughout the section, especially surrounding the invading tumor tissue.

The liver shows no changes aside from a moderate degree of fatty infiltration and deposition of a brown pigment in the liver cells. The nuclei stain well everywhere with hæmatoxylin.

The gall-bladder specimen was lost, but showed no changes anatomically.

Sections of lung and the tumor in the omentum were stained by Weigert's method for elastic fibres. These sections show plainly that the elastic fibres have extensively proliferated. Everywhere throughout the section from an area of consolidation in the lung the heavy bands of connective tissue forming the stroma are rich in elastic fibres. That the alveolar wall forms in many places the stroma of the tumor is now very evident, as the elastic fibres normally present still hold their general appearance in the alveolar septa.

The omental tumor shows the absence of elastic fibres except in the bloodvessels and their immediate vicinity; only rarely do they extend into the stroma, and when fibres are thus seen they are very thin.

That the elastic fibres proliferate in the process of endarteritis obliterans is plainly shown; a very fine fibrillary network of elastic fibres is seen branching from the internal elastic lamina and extending into the thickened intima for some distance, but nowhere does it reach the extreme inner margin.

The tumor-like proliferation of endothelium described as occurring in the right lung does not present the same picture, but shows that the elastic fibres have not proliferated to any considerable degree.

The autopsy and the microscopic study show the source of all the clinical symptoms and findings. The only question left to answer is, Where and how did this tumor originate? The history of this case does not show any previous disease of the lung or bronchi with subsequent scar formation, such as tuberculous or syphilitic ulcers, the scars of which are supposed to be predisposing factors in the etiology of bronchial cancer. The duration of the disease was rather long—almost two years, if we assume that the first symptoms were due to cancer. The character of the epithelium of the tumor is such that it may have originated from a bronchus, and in one place I have described a node projecting into the lumen of a bronchus, which may have been the origin of the tumor. This is not certain, however. There is no evidence of carcinoma elsewhere in the body except the thickening of the diaphragm, which is due to carcinoma, and the tumor in the omentum. Such a tumor could not originate in the omentum. Taking into consideration the fact that no tumor was found in the stomach, liver, pancreas, kidneys, and intestines, and that the symptoms from the start were directly referable to the left lung, where the tumor was found, I believe we have sufficient evidence to say that this is probably a primary cancer of the lung. There is no likelihood that it was secondary to a tumor which remained dormant during the two years of her sickness. Primary carcinomata of the lung are rare, but not exceptional. In reading the literature there are perhaps more than seventy-five well-reported and credible primary carcinomata of the lung. The symptoms, course, findings, and general picture of this case correspond with those reported by other observers. This case is reported because it has considerable clinical and pathological interest, and in the hope of encouraging fuller reports of such exceptional cases.

THE MOVEMENTS OF SUPERIOR INTERCOSTAL MUSCLES IN HEMIPLEGICS.

By L. Pierce Clark, M.D.,
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The present accepted opinion of the respiratory movements in hemiplegics is well stated by Gowers,[1] who says that "The two sides of the thorax move equally in ordinary respiration, but if the patient

[1] Diseases of the Nervous System, vol. ii. p. 75.

takes a deep breath and brings into action the extraordinary muscles of respiration the half of the thorax on the paralyzed side often expands less than the other. Thus, some muscles are completely paralyzed, others are merely weakened, others are apparently unaffected."

These rules are based upon the well-known Broadbent hypothesis, that bilaterally acting muscles are represented bilaterally in the cerebral cortex. There is a failure to note, however, that the movements on the sound side in extraordinary respiration are *always* greater, which modifies Broadbent's hypothesis so to state that even bilaterally acting muscles, although represented bilaterally, are represented contralaterally to a greater degree.

In 1895 Hughlings Jackson[1] stated that the superior intercostals play a more or less constant rôle in the syndrome of hemiplegics, contrary to the universally accepted opinion as given in quotation from Gowers. He believed that in ordinary or automatic respiration the amplitude of superior intercostal movements was greater on the paralyzed side than on the other; while in volitional (cerebral) movements, such as that of forced conscious or extraordinary respiration, the usual law of greater movements of the sound side would be found. To substantiate this he reported observations on twenty-eight cases of old and recent hemiplegics, in which the greater number of cases (eighteen in twenty-eight) proved the accuracy of his theory.

Recently I had opportunity to re-examine some cases that were thought to negative the law, but after giving considerable attention to the necessary technique I found they were no exceptions to the law. I have furthermore examined 161 cases of hemiplegia in the Craig Colony, in hospitals, and at the Vanderbilt Clinic of this city, to make certain the constancy of this respiratory symptom in hemiplegics. The value of the sign if present in all destructive capsular lesions is obvious. I examined 120 consecutive cases of the series of 161, and the remainder were made under my direction.[2]

As a result of this clinical study I found the sign uniformly present in all without any apparent relationship to age, character, duration, or severity of capsular lesion (aside from its being hemiplegic in range). The double change (first, overaction on paralyzed side in automatic respiration, and the second shown in the converse in extraordinary or volitional respiration) was very marked in some and very slight in others; the difference, however, was only one of degree. In all cases the symptom can be detected by palpation, and in most cases even by inspection alone.

The explanation for the phenomenon is as follows: In destructive

[1] Lancet, February 23, 1895, Neurological Fragments, No. 15.

[2] I am particularly indebted to Drs. Witmer, Young, Palmer, and Shanahan for assistance in collecting data for this clinical report.

lesions of the internal capsule causing paralysis, hemiplegic in character, the cortical inhibitory control over the medullary respiratory centre of the paralyzed side is destroyed in greater part, at least, much more so on the hemiplegic side than to that centre presiding over the sound side; in consequence of this withdrawal the uninhibited medullary centre overacts in automatic or ordinary respiration, hence the excess movements on the paralyzed side. But in forced conscious or volitional (cerebral) respiration the movements of the thorax on the opposite sound (or nearly so) side are greater.[1]

As to the location of the inhibition centre for respiration in the cortex, W. G. Spencer[2] has demonstrated by electrical stimulation of the cortex in monkeys that slowing and final arrest of respiratory rhythm was produced by excitation of the cortex just outside the olfactory tract, in front of the point where it joins the temporosphenoidal lobe, and the nerve fibres from this region run in a parallel direction with fibres of the olfactory limb in the anterior commissure; after decussating here the tract is continued backward on either side of the infundibulum into the red nucleus below and external to the aqueduct at a plane of the exit of the third nerve. Therefore, we must have a destruction of this centre or its tract in the capsular lesion which results in automatic overaction of superior intercostals on the paralyzed side. (The many interesting speculations relating to the connection between the sense of olfaction and that of cortical respiratory inhibition are at once suggested.) Furthermore, it should be noted that Spencer's valuable and carefully conducted experiments show an acceleration centre which must remain intact and operative in the hemiplegics. In locating the last-named centre in the monkey's cortex he demonstrated that increased action or respiratory acceleration resulted by electrical stimulation of the posterior portion of the sensorimotor area of the cortex. Fibres from this centre were followed back just below the lenticular nucleus where it borders on the outer and ventral portion of the internal capsule; they run at first external and then ventral to the motor portion of the internal capsule, and so reach the tegmentum. The tract from the two sides meet in the interpeduncular gray matter at the level of and just behind the exit of the third nerve. The exact manner in which these cerebral tracts join the respiratory nucleus has not yet been determined either experimentally or pathologically. Even the motor cerebral distribution to the third, fourth, sixth, ninth, and tenth has not yet been worked out. But that they possess as definitely a cerebral supply as the remaining cranial nerves may be con-

[1] In a later communication Jackson states that inasmuch as he did not find the symptom present in every case there were many difficulties to the acceptance of the hypothesis for even some cases of hemiplegia.

[2] Lancet, December 16, 1899.

jectured. Barnes[1] has recently suggested that the cerebral motor supply to the ninth and tenth cranial nerves may be through Pick's bundle, a course which, if true, must be entirely different from that given by Spencer's respiratory tract.

Of Spencer's two centres the inhibitory one is anterior and internal, and consequently its damage would be expected in vascular lesions, especially of the middle cerebral artery affecting the integrity of the capsular fibres, while the acceleration centre is posterior and external to the capsule and might easily remain unimpaired.[2] On the whole, Spencer's work explains the new respiratory symptom in hemiplegics. The fact that the superior intercostals of the paralyzed side are enervated through cerebral fibres ending on spinal centres in the anterior horns of the cord, and the more or less marked damage of the same will account for the general motor loss of volitional acts on the hemiplegic side. To further substantiate the anatomical fact of a double enervation of the intercostals, Jackson has suggested also that the increased respiration in early stages of surgical anæsthesia is owing to impairment or loss of function of Spencer's cortical arrest centres. I have seen one case of double hemiplegia (paralysis on the two sides occurring three days apart) in which there was typical acceleration of respiration so marked in degree that the house physician noted the patient appeared as "though going under an anæsthetic." Another case of double hemiplegia did not show this (since the lesion on the two sides was sustained several years apart and adaptation to the first lesion had taken place before the second occurred). The respiratory symptom was present on the side most paralyzed, although it was slight, as would be expected. In the status epilepticus increased respiratory frequency is commensurate with the degree of general cerebral exhaustion, an analogue of general anæsthesia so far as the inhibitory power of the cortex is concerned; finally, Cheyne-Stokes respiration occurs frequently in status without prognosis being so grave as in the other conditions of its occurrence.

The principle underlying the respiratory sign has a wider application than was first thought; it may be demonstrated in any and all muscles bilaterally susceptible of both automatic and volitional movements. It occurs in the seventh cranial nerve in volitional and emotional acts, where it is well known that a slight movement is more conspicuous on the parts paralyzed on the affected side, while a strong one is far less in degree. It also occurs in the action of the third division of the fifth nerve (masseters), and in the act of swallowing, the function of the ninth cranial.

[1] Brain, Winter Number, 1902.

[2] It is just possible that the accelerator centre may be involved in those very posterior lesions of the capsule and thus negative the law in rare cases, but I have not seen such a case as yet.

In many cases it is possible to demonstrate definitely by palpation the inclusion of all chest muscles on the paralyzed side in the new phenomena noted alone for the superior intercostals. I am certain more careful means for detecting this slight difference will show that all the so-called muscles of ordinary respiration enter the hemiplegic syndrome. Jackson mentions one case illustrating this fact which was observed by him.

The necessity for accurate confirmation of the exact location of Spencer's two respiratory centres by means of degeneration experiments and the course which tracts take from such centres to the respiratory nucleus in the medulla is obvious.

A NOTE ON THE FOOT OF THE AMERICAN NEGRO.[1]

By Albert H. Freiberg, M.D.,
and
J. Henry Schroeder, M.D.,
of Cincinnati, Ohio.

It would appear that the widespread notion of the flatness of the negro's foot had its origin in this country. The bones of the negro's normal foot differ in no regard from the white man's as far as their individual shapes are concerned, excepting that of the os calcis, the length of whose posterior process is admittedly greater in the negro. Nevertheless, the flatness of the negro's foot has become proverbial, and has given rise to the saying that "the hollow of his foot makes a hole in the ground." As a racial characteristic of the aboriginal negro, the flatness of the plantar arches has been disproved by Herz and Muskat in recent publications. The former has shown conclusively in a large number of observations made in Africa that a well-developed and easily apparent plantar arch exists far more constantly in the negro as there found than in an equal number of Europeans. While this is doubtless true, there can, on the other hand, be little uncertainty that the homely observation of the contrary condition in the American negro has some basis in fact. Abundant opportunity for superficial examination of adult negro feet in this country brings with it the impression that flat foot is present in the negro with unusual frequency as compared with the white. The present investigation is offered as incomplete, in so far as the number of observations is too small for binding conclusions, but as being rather convincing in its results, nevertheless.

[1] Presented to the American Orthopedic Association, May, 1903.

There were used as material for the observations herewith presented eighty-eight feet of adult negroes who were walking patients in the wards of the Cincinnati Hospital. A large proportion of them were under treatment for venereal disease. Eight of these forty-four were women. The men were practically all engaged in heavy laboring occupations. Impressions of the feet were taken by the iron and tannic acid method. Attention was paid particularly to the flatness as shown by the impression and to the condition of the great toe. Of this series but 16.2 per cent. of the feet lacked both hallux valgus and marked flattening of the arch. Hallux valgus without descent of the arch was present in 27 per cent., while marked flat foot was observed in 56.8 per cent. Of the cases of flat foot 92 per cent. had accompanying hallux valgus.

For the sake of comparison a series of impressions of the feet of white patients was taken. Their occupations were noted and were found to be about the same as those of the negroes. Thirty-four feet were examined in twelve men and five women. Of this number 59.2 per cent. had neither hallux valgus nor flat foot. Hallux valgus without flat foot was present in 35 per cent., while but 5.8 per cent. had flat foot, being two cases in both of which hallux valgus was present. It was furthermore noted that 41 per cent. of the white feet presented hallux valgus, with or without flatness, while in the negroes this percentage was 79.5. This frequency of hallux valgus seems of special importance, since it may be considered purely as the result of deforming foot gear.

Although, as before remarked, the number of observations is too small for definite conclusions, the variation in the figures is quite striking. Not only is flat foot much more common in the negro, comparatively speaking, but distortion of the great toe is relatively twice as frequent as in the white.

In the belief that an interesting comparison would result, impressions were taken of the feet of twenty colored children between the ages of thirteen and three years. Of the forty feet examined 75 per cent. had normal feet; 25 per cent. had flat foot, of which 80 per cent. were associated with hallux valgus. Hallux valgus was present in 25 per cent. of the whole number.

By far the greater number of negroes in Cincinnati have more or less admixture of white blood in them. On this account note was made of the color of all the adult negroes examined. There were noted as dark 34, as of medium or light color 54. Of those noted as dark 53 per cent. had flat foot and 70.5 per cent. had toe valgus. Of those classed as medium and light 59 per cent. had flat foot, while 87 per cent. had toe valgus. It would thus appear that these deformities were somewhat more frequent in the lighter colored than in the dark,

although the difference cannot be considered great. In fact it appears that, considering the small number involved, this difference can be ignored.

Were the number of observations sufficiently large it would seem justifiable to draw the following inferences:

1. Flattening of the arch of the foot is much more frequent in the American negro than in his white neighbor.

2. Hallux valgus is likewise more frequent in the negro than in the white American.

3. The well-arched foot occurs in the American negro with sufficient frequency to establish it as the normal.

4. While flattening of the arch is more common in the negro child than in the white, the normal foot preponderates decidedly.

5. From this it would be fair to conclude that the flat foot of the adult American negro has developed after the period of childhood in the greater number of cases.

6. The deforming effects of footwear are much more evident in the adult negro than in the white man of the same class. This is shown by the fact that decided valgus of the great toe is much more frequent.

There require to be explained the cause of the frequency of flat foot in the negro child and its increase in adult life. The great frequency of rickets in negro children is well recognized, and its manifestation in bowlegs and knock-knee is quite familiar. This alone would account for a considerable portion of the flat foot in children. However, it will be noted that even in these hallux valgus was present in 80 per cent. of the flat-footed. This, together with the marked frequency of hallux valgus in the adult, would make it seem likely that the effect of shoes in distorting the feet is especially marked in the negro, both child and adult. This might be explained by the fact that the negro foot is wide in its anterior portion, and, therefore, especially prone to compression. The length of the heel would, however, seem also to merit consideration. It would have the effect of shortening the shoe for the forepart of the foot, since it virtually displaces the ankle forward.

It would seem that a negro's foot cannot be covered with a white man's shoe with impunity.

Should future investigation agree with the above findings it would become necessary to abandon the idea that a flat plantar arch is an hereditary and racial characteristic of the American negro, but this condition would have to be regarded, in part at least, as the injurious result of shoes of improper construction.

The excuse for presenting so incomplete an inquiry is to stimulate further research into a question of importance, not only in its purely

ethnological aspects, but also as it pertains to the theory of development of one of the most frequent deformities of all civilized people.

	Adult negro.	*Adult white.*	*Negro children.*
Number of feet examined	88	34	40
Percentage of flat feet	56.8	5.8	25
Hallux valgus without flat foot	27.0 per ct.	35.0 per ct.	5 per ct.
Without flat foot or hallux valgus	16.2 "	59.2 "	75 "
Hallux valgus present in	79.5 "	41.0 "	25 "
Of flat feet hallux valgus present in	92.0 "	100.0 "	80 "

STUDIES ON THE ANTAGONISTIC ACTION OF DRUGS.

By H. D. Haskins, M.D.,
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WITH AN INTRODUCTION BY TORALD SOLLMAN, M.D.

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I. Introduction.

The question whether a drug which excites a given structure can remove the effects of another drug which depresses the same structure cannot be considered as answered. Recent evidence—as the work of J. C. Rothberger[1] on the antagonism of physostigmine and curare, and that of A. P. Mathews[2] on atropine and pilocarpine, and that of Stokvis[3] on digitalin and quinine—favors this view, without being entirely decisive. Accepting the theoretical possibility that an excitant can remove the symptoms produced by a depressant, there still remains the question whether the excitant really removes the depression or whether it only masks it through the excitation. It would seem, *a priori*, that the former can only be the case when the excitant prevents the depressant from combining with the protoplasm, as, for instance, when an alkali prevents the action of an acid. In these cases the antagonism is chemical or physical. If, however, both the depressant and the excitant combine with the protoplasm, as is supposed to be the case when, for example, pilocarpine and atropine act simultaneously, it must be assumed that they both produce their action. If in this case no noticeable phenomena result, this is not because the drugs exert no action, but because the resultant of the actions is zero. For example, it is quite easily conceivable that a cell depressed through starvation may be restored temporarily to its original activity, say by an increase of temperature, and may for a time behave like a normal cell. Nevertheless, it is far from normal; it will probably show chemical, functional, and structural changes, and will, for instance, fatigue

[1] Pflüger's Archiv, 1901, Bd. lxxxvii. p. 117.
[2] American Journal of Physiology, vol. vi. p. 207.
[3] Virchow's Festschrift, 1891, Bd. iii. p. 349.

more readily. Similarly, if we assume that the biogen-pilocarpine compound functionates very actively, the biogen-atropine compound very sluggishly, then the biogen $\begin{cases} \text{atropine} \\ \text{pilocarpine} \end{cases}$ compound may functionate very nearly like the free biogen molecule. Nevertheless, a chemical difference must exist between the compound and the free biogen molecule, and this difference must entail other differences in the chemistry, functions, or morphology of the cell. The discovery of such differences in cases in which a complete physiological antagonism is assumed would go far to support this thesis.

Dr. Haskins, at my suggestion, undertook the investigation of some such phenomena, the results of his work being detailed in the following papers:

The histological changes which alcohol is believed to produce in nerve cells seemed to offer a fit object for this study, the question being, Whether a drug which lessens the toxic effects of alcohol also lessens the histological lesions. Since strychnine is credited with counteracting the physiological effects of alcohol, it was chosen as an antidote. It may be said at once that the results throw no light upon the question: first, because the alcohol did not produce the lesions which are credited to it; and, secondly, because strychnine did not prove to be very efficient in preventing the alcohol symptoms. The data seem of sufficient practical interest in other directions to merit reporting.

It was then planned to investigate the subject along an entirely different line, by studying the effect of the simultaneous action of stimulants and depressants on yeast cultures. As no reliable stimulant could be found among drugs, various degrees of heat were resorted to, and were contrasted with the depressant action of strychnine. The results show that the antagonism is far from being as simple a phenomenon as one would expect if the stimulant action of heat neutralized the depressant effect of strychnine. They are more in agreement with the complicated condition which would obtain if the stimulation and depression were superimposed. It must be granted that the stimulation by heat may be of quite a different nature from stimulation by drugs. It must also be granted that there may be various types of physiological antagonism among drugs. These are matters which cannot be considered as definitely settled until a large number of antagonisms have been studied in detail.

II. The Effect of Strychnine on Alcohol Poisoning.

Experiment 1. Summary. Two guinea pigs were each given 40 c.c. of 40 per cent. alcohol per kilo body-weight by intraperitoneal injection, divided into seven doses, during a period of twelve hours. This sufficed to kill one of them. The surviving guinea-pig had been given

in addition to the alcohol 0.15 mg. of strychnine sulphate per kilo weight subcutaneously in a 1 : 20,000 solution, also divided into seven doses.

Protocol. Two healthy guinea-pigs were selected—A, weighing 290 gm.; B, 350 gm. 8 A.M., 10 c.c. of 40 per cent. alcohol per kilo weight injected into A and B; also 0.1 mg. of strychnine sulphate per kilo weight into B. Ten minutes later B lies in a stupor and has rhythmical tremors of the legs. One hour after injection, B the same; A has shown little effect from the alcohol aside from restlessness and occasional shivering; respiration of A, 65; of B, 85 per minute. Two hours after injection A has almost recovered from his indisposition, while B has but partially recovered.

10 A.M., the second injection: A and B are given 5 c.c. of 40 per cent. alcohol per kilo weight; B also 0.025 mg. of strychnine sulphate per kilo weight. Five minutes later A has become indisposed, B lies in complete stupor, and exhibits the same tremors. During the next hour A gradually becomes partly paralyzed so that he cannot stand nor walk; B remains the same as before. Respiration of A keeps at about 60, of B at 70 per minute. Finally A lies over onto his side in a stupor, and has tremors of exactly the same rhythm as B. Four and one-half hours after the injection both have recovered considerably, but A is more relaxed and indisposed than B.

2.30 P.M., the third injection: A and B receive 5 c.c. of 40 per cent. alcohol per kilo weight; B also receives 0.0125 mg. of strychnine sulphate per kilo weight. A becomes narcotized much more quickly than B. Fifteen minutes after injection both present the same symptoms as after the previous injection, namely, stupor and tremors. Respiration of A is 40, of B 80 per minute. Two and one-half hours after injection they are in the same condition.

5 P.M., the fourth injection of the same dosage as the third. Within a few minutes A ceases to have tremors and begins breathing by gasps. One and one-half hours after injection A seems to be paralyzed completely as far as voluntary muscles are concerned, since he lies relaxed and motionless. Respiration of A is 28, of B 65 per minute. B lies in the same condition as before.

7 P.M., the fifth injection: A and B receive 5 c.c. of 40 per cent. alcohol per kilo weight. No more strychnine is given.

7.20 P.M., the sixth injection, same as fifth.

7.30 P.M., the seventh injection, same as fifth and sixth. Respiration of A is 10, of B 17 per minute. A is evidently almost dead. B is weaker, but has the leg movements still.

8 P.M., A is dead; B is alive and not fully paralyzed. B is killed. Both animals are dissected and portions of the central nervous system removed for histological examination.

Experiment 2. Summary. Two cats were each given intraperitoneally 20 c.c. of 40 per cent. alcohol per kilo body-weight in two doses of 10 c.c., five and one-half hours apart. One cat received in addition 0.1 mg. per kilo weight of strychnine sulphate in 1 : 20,000 solution subcutaneously in three doses. The latter died during the night. The other cat died forty-six and one-half hours after the first injection.

Protocol. Two cats were taken, Cat 1 weighing 2980 gm., Cat 2 2180 gm. Cat 2 was not perfectly healthy, as evidenced by a discharge from the eyes.

9 A.M., Cat 1, pulse 100, respiration 40. Cat 2, pulse 108, respiration 48.

9.30 A.M., first injection intraperitoneally into Cat 1 and Cat 2 of 10 c.c. of 40 per cent. alcohol per kilo weight and 0.025 mg. of strychnine sulphate per kilo weight subcutaneously into Cat 2. Seven minutes later Cat 1 shows beginning narcosis. Thirteen minutes are required to make Cat 2 lie down quietly. Fifty minutes after the injection, pulse of Cat 1 is 96, of Cat 2 is 100 per minute; both are completely paralyzed in the hind legs. One and one-half hours after injection both lie quietly sleeping, Cat 1, pulse 100, respiration 80; Cat 2, pulse 120, respiration 45. Two hours after injection Cat 2 receives another dose of strychnine of the same size as before. Two and one-half hours after first injection, Cat 1, pulse 120, respiration 68; Cat 2, pulse 120, respiration 36. Five hours after injection Cat 1 shows partial recovery. Cat 1, pulse 120, respiration 52; Cat 2, pulse 120; respiration 36.

3 P.M., second injection into Cat 1 and Cat 2 of 10 c.c. of 40 per cent. alcohol per kilo weight and of 0.05 mg. of strychnine sulphate into Cat 2. Both lie relaxed within a few minutes. Fifteen minutes after injection, Cat 1, pulse 120, respiration 72; Cat 2, pulse 120, respiration 48. One and one-quarter hours after injection both lying unconscious still. Cat 1, pulse 120, respiration 68; Cat 2, pulse 120, respiration 32. One-quarter of an hour later Cat 2 begins to gasp, and respiration stops within a few minutes, then begins again at the rate of 16 per minute.

Cat 2 died during the night.

Cat 1 lay unconscious all the next day, but could be aroused somewhat; the respiration varied from 44 at 8 A.M., 26 at 2.30 P.M., to 34 at 4.30 P.M. At 7.30 the next morning he was breathing feebly. Cat 1 died at 8 A.M.

Experiment 3. Summary. Two cats were each given 20 c.c. of 40 per cent. alcohol per kilo body-weight intraperitoneally in two equal doses, twenty-four hours apart. One died twenty-six and three-quarter hours after the first injection. The survivor had received 0.15 mg. of strychnine sulphate per kilo body-weight in six doses.

Protocol. Two healthy cats were taken, Cat 1 weighing 2700 gm., Cat 2, 2610 gm.

9 A.M., Cat 1, pulse 140, respiration 36; Cat 2, pulse 140, respiration 42. First injection: Cat 1 and Cat 2 receive 10 c.c. of 40 per cent. alcohol per kilo weight intraperitoneally; Cat 2 gets 0.025 mg. of strychnine sulphate solution 1 : 20,000 subcutaneously. Four minutes after injection both are lying on the side. Twelve minutes after injection, Cat 1, pulse 140, respiration 78; Cat 2, pulse 140, respiration 78. Forty-five minutes after injection, Cat 1, pulse 140, respiration 92; Cat 2, pulse 140, respiration 120. One hour after injection Cat 2 is given another dose of strychnine of the same size. Both make movements occasionally. One and one-half hours after first injection, Cat 1, pulse 140, respiration 64; Cat 2, pulse 140, respiration 80; both are sleepy. Two and one-quarter hours after injection, gave the third dose of strychnine to Cat 2. Two and one-half hours after first injection both appear exactly as if merely asleep. Cat 1, pulse 140, respiration 64; Cat 2, pulse 140, respiration 56. Five hours after injection both asleep. Cat 1, pulse 140, respiration 46; Cat 2, pulse

140, respiration 36. Fifteen minutes later another dose of strychnine to Cat 2. Five and three-quarter hours after first injection Cat 1 moves about, using the front legs, the hind legs still being useless. Cat 1, respiration 44; Cat 2, respiration 40. Six and one-half hours after injection another dose of strychnine to Cat 2. Forty-five minutes later, Cat 1, pulse 120, respiration 40; Cat 2, pulse 120, respiration 28. Cat 1 is more conscious and more desirous of moving about than Cat 2. The next morning both were alive and conscious. Cat 2 seems to be more vigorous than Cat 1, for he will walk about.

9 A.M., Cat 1, pulse 140, respiration 28; Cat 2, pulse 140, respiration 36. Second injection the same as the first. Twenty minutes later both lie quiet. Cat 1, pulse 140, respiration 28; Cat 2, pulse 140, respiration 80. One hour after injection, Cat 1, pulse 142, respiration 42; Cat 2, pulse 140, respiration 44; Cat 2 more conscious than Cat 1. Two and one-quarter hours after injection Cat 1 begins to gasp. Five minutes later Cat 1 dies; Cat 2 is asleep, pulse 140, respiration 28. Allowed Cat 2 to live one and one-quarter hours longer; pulse and respiration remained unchanged; made voluntary movements and reacted to pain.

Experiment 4. Summary. The effect of strychnine in counteracting alcohol when given in smaller doses during a longer period was tested in this experiment. Two kittens were each given 35 c.c. of 20 per cent. alcohol and 105 c.c. of 40 per cent. alcohol per kilo body-weight during thirteen days, and one of them received 3.1 mg. of strychnine sulphate per kilo weight in 1 : 5000 solution in addition to alcohol. Neither cat died. The cat that received strychnine showed a somewhat greater paralytic effect at the end of the experiment.

Protocol. Two healthy and lively kittens were taken, Cat 1 weighing 930 gm., Cat, 2 910 gm.

First day, 12.45 P.M., subcutaneous injection of 0.1 mg. per kilo weight of strychnine sulphate into Cat 2. Twenty-five minutes later noticed increased reflex excitability, for Cat 2 would start up as if struck at every sudden sound.

2 P.M., injected 5 c.c. of 20 per cent. alcohol per kilo weight subcutaneously into Cat 1 and Cat 2. Twenty-five minutes after injection both are lying down, sleeping lightly. Cat 1, respiration 28; Cat 2, respiration 19; Cat 2 still excitable.

3 P.M., another injection of alcohol, same as before, and a second dose of strychnine to Cat 2. Excitability of Cat 2 has decreased. Thirty minutes after injection excitability of Cat 2 is again increased; both asleep; respiration of Cat 1 is 30, of Cat 2, 23.

4 P.M., neither seem to be under the influence of the alcohol.

Second day, 9 A.M., both are normal; eat and drink heartily. Cat 2 shows no increased reflex excitability.

9.30 A.M., injection of 5 c.c. of 20 per cent. alcohol per kilo weight subcutaneously into Cat 1 and Cat 2, and of 0.1 mg. of strychnine sulphate per kilo weight into Cat 2. Thirty minutes later neither show any alcohol effect. Cat 2 begins to manifest increase of excitability; respiration of each is 36 to 40.

10 A.M., second injection same as first. Thirty minutes later both are less lively, Cat 2 more restless than Cat 1.

11 A.M., third injection, same as before. Fifteen minutes later both are sleepy. Twenty-five minutes after the injection neither cares to

move about; respiration of each 40 to 48. When roused up Cat 1 shows weakness of the hind legs; Cat 2 does not. Four hours after injection both have almost recovered.

3.30 P.M., fourth injection, same as before. One hour after injection both are sleepy, but can walk naturally when aroused; Cat 2 still shows increase of excitability.

Third day, 8.30 A.M., both seem normal; eat and drink freely.

8.40 A.M., first injection, same as on the day before. Thirty minutes later no effect noticeable.

9.20 A.M., second injection, 5 c.c. of 40 per cent. alcohol per kilo weight, subcutaneously into Cat 1 and Cat 2 and 0.1 mg. of strychnine sulphate per kilo weight into Cat 2. Forty minutes later both are asleep.

10.40 A.M., third injection, same as second. Cat 2 becomes very restless within a few minutes. Thirty minutes after injection both lie quietly; Cat 2 is more excitable than he has been. Forty-five minutes after injection both are disposed to lie still, but can walk with a wobbling gait when aroused. Three and one-half hours after injection both are sleepy; respiration 34 to 36; both show partial paralysis of the hind legs, tending to stagger and fall over onto the hip in walking. Thirty minutes later an extra dose of strychnine to Cat 2.

4 P.M., both are asleep; can walk better; Cat 2 is slightly excitable.

Fourth and fifth days: No drugs were administered.

Sixth day: Kittens are normal.

9.40 A.M., injection of 0.1 mg. of strychnine sulphate per kilo weight into Cat 2.

10.12 A.M., injection of 5 c.c. of 40 per cent. alcohol per kilo weight into Cat 1 and Cat 2.

10.55 A.M., second injection of alcohol and strychnine in the same doses as before. Twenty minutes later both are lying down. Four and one-half hours after injection Cat 1 seems to be sleepier than Cat 2; Cat 2 is less excitable than usual.

3.30 P.M., injection of an extra dose of strychnine into Cat 2. Twenty minutes later Cat 2 shows increased excitability.

4 P.M., third injection, same as second. Fifteen minutes later both stagger when they walk.

Seventh day: No drugs given. Eighth day: Both seem normal; have good appetite.

2.15 P.M., injection of 10 c.c. of 40 per cent. alcohol per kilo weight into Cat 1 and Cat 2, and of 0.2 mg. of strychnine sulphate per kilo weight into Cat 2. Twenty minutes later both are sleepy; Cat 2 is not excitable.

3.30 P.M., second injection, 5 c.c. of 40 per cent. alcohol per kilo weight, into Cat 1 and Cat 2; 0.2 mg. of strychnine sulphate per kilo weight into Cat 2. Thirty minutes later both are lying quietly; both stagger when made to walk; Cat 2 walks steadier than Cat 1.

Ninth day: Neither is lively; can walk, but is indisposed to. Cat 2 seems sicker than Cat 1.

9 A.M., injection of 10 c.c. of 40 per cent. alcohol per kilo weight, subcutaneously into Cat 1 and Cat 2, and of 0.2 mg. of strychnine sulphate per kilo weight into Cat 2. Twenty-five minutes later both are lying down asleep. Two and one-quarter hours after injection both can walk about; neither would eat much meat.

11.15 A.M., second injection, 5 c.c. of 40 per cent. alcohol per kilo weight, into Cat 1 and Cat 2; 0.1 mg. of strychnine sulphate into Cat 2. Three and one-quarter hours later neither can walk well; Cat 1 is steadier than Cat 2; Cat 2 is very sleepy and shows no increase of reflex excitability.

3.20 P.M., extra dose of strychnine to Cat 2. Twenty minutes later Cat 2 shows slight excitability.

4.35 P.M., third injection, same as second.

Tenth day: Cat 2 is more indisposed than Cat 1. They have eaten the meat left in the cage the evening before.

9.20 A.M., injection of 10 c.c. of 40 per cent. alcohol per kilo weight into Cat 1 and Cat 2, and of 0.2 mg. of strychnine sulphate per kilo weight into Cat 2. Reweighed them: Cat 1 weighs 1060 gm., Cat 2 960 gm., Cat 1 having gained 130 gm. and Cat 2, 50 gm. in eight days. One and one-half hours later Cat 2 is more profoundly asleep than Cat 1; respiration of Cat 1 is 36, of Cat 2, 22.

3 P.M., second injection, 5 c.c. of 40 per cent. alcohol per kilo weight, into Cat 1 and Cat 2; 0.1 mg. of strychnine sulphate per kilo weight into Cat 2. Twenty minutes later Cat 1 walks unsteadily; Cat 2 cannot walk.

Eleventh day: No drugs given. Twelfth day: Both seem to have recovered; Cat 1 is livelier than Cat 2.

11.25 A.M., injection of 10 c.c. of 40 per cent. alcohol per kilo weight into Cat 1 and Cat 2, and of 0.2 mg. of strychnine sulphate per kilo weight into Cat 2. Two and one-half hours after injection they have recovered partially from the alcohol.

2.15 P.M., second injection, 5 c.c. of 40 per cent. alcohol per kilo weight, into Cat 1 and Cat 2; 0.1 mg. of strychnine sulphate into Cat 2. One hour later Cat 2 is soundest asleep and weakest when it tries to walk.

3.30 P.M., third injection, 10 c.c. of 40 per cent. alcohol per kilo weight, into Cat 1 and Cat 2; 0.1 mg. of strychnine sulphate into Cat 2. Forty minutes later both show the most marked paralytic effect yet obtained. Cat 1 can only crawl a little when aroused; Cat 2 lies perfectly relaxed and cannot be made to move.

Thirteenth day: 9.30 A.M., both cats are still narcotized. Cat 2 is still paralyzed, more than Cat 1. Respiration of Cat 1 is 19, of Cat 2 12. Weight of Cat 1 is 1060 gm., of Cat 2 is 910 gm., Cat 1 being of the same weight as on the ninth day, Cat 2 being 50 gm. lighter.

10.30 A.M., intraperitoneal injection of 5 c.c. of 40 per cent. alcohol per kilo weight into Cat 1 and Cat 2; 0.1 mg. of strychnine sulphate per kilo weight into Cat 2. Neither gave evidence of pain from this injection.

3.15 P.M., Cat 1, pulse 130, respiration 28; Cat 2, pulse 130, respiration 20. Both are almost comatose.

3.30 P.M., killed both kittens.

III. Does Acute and Subacute Alcohol Poisoning Lead to Histological Changes in Nerve Cells?

Method of Investigation. Pieces of the spinal cord, cerebellum, and cerebrum from corresponding locations were removed from guinea-

pigs A and B of Experiment 1, and also from a normal guinea-pig. They were then fixed and hardened in absolute alcohol; sections were cut without embedding, and stained by Nissl's method on the same slides, as directed by C. C. Stewart.[1]

The same course was pursued with Cat 1 of Experiment 2 and Cats 1 and 2 of Experiment 3; also a normal cat. The tissues taken from the two kittens of Experiment 4 were fixed in 10 per cent. formalin, then put through graded alcohols and embedded in celloidin. The sections were stained with erythrosin, then with Nissl's methylene blue, as directed by F. R. Bailey.[2]

Results. The nerve cells of normal and drugged animals were not distinguishable the one from the other; all stained beautifully and showed no injury to nucleus or nucleolus. In all the sections the Nissl bodies or granulations of the large nerve cells were distinct and numerous. Only in extra thin portions of the sections were these granulations less numerous. No constant difference was observable between nerve cells from the normal and from the poisoned animals. It was, therefore, impossible to corroborate the results reported by C. C. Stewart.

IV. The Influence of Certain Drugs upon the Quantity of Gas Formed by Yeast.

Method of Experimentation. Fermentation tubes were used, the amount of gas formed from a given amount of glucose solution by the action of yeast within a given time being estimated. The ordinary method was found to be too unreliable, and it was modified as follows: The upright limb of the fermentation tube was filled about half-full with mercury, then, while the tube was still held inverted, a measured quantity (usually 2 c.c.) of a 5 per cent. solution of pure glucose in distilled water was run in on top of the mercury by means of a pipette, and was followed by an equal quantity of yeast mixture (usually 10 per cent. of compressed yeast suspended in distilled water), then the tube was immediately placed upright and all of the glucose-yeast mixture drawn up above the mercury by tilting the tube slightly so that it was sucked up out of the neck by capillarity. The tubes were kept in an oven at 35° to 40° C. during the period of gas formation. Drugs were dissolved in the glucose solution before the latter was put into the tubes. Each drugged tube was accompanied by an undrugged tube as a control, which was filled at the same time and contained the same amount of glucose and yeast as its fellow. The reading of the amount of gas formed in the two tubes was made before the mercury

[1] Journal of Experimental Medicine, vol. i., No. 4. [2] Ibid., vol. v. p. 549.

TABLE I.—EFFECT OF DRUGS ON GAS FORMATION BY YEAST IN 2½ PER CENT. GLUCOSE AT 40° C.

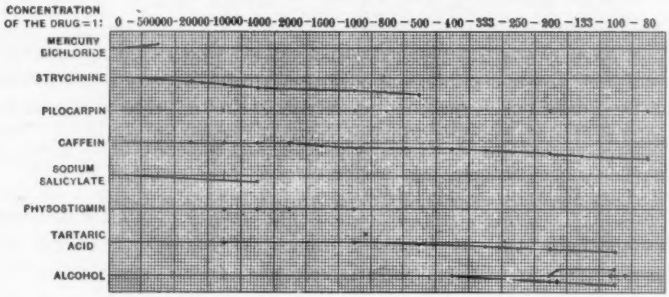
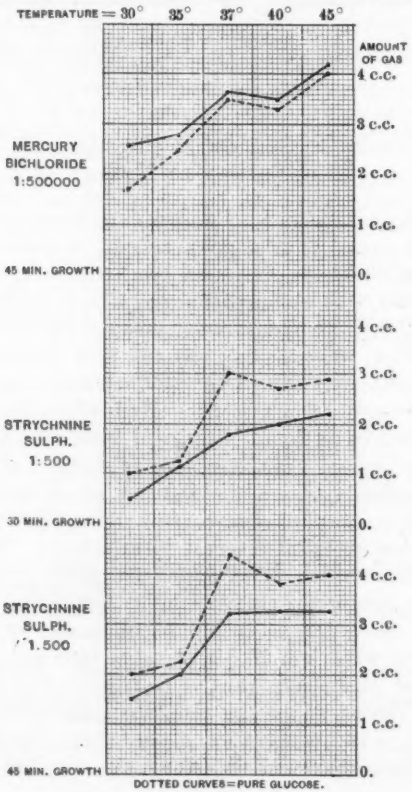

CONCENTRATION OF THE DRUG = 1:
0 – 500000 – 20000 – 10000 – 4000 – 2000 – 1600 – 1000 – 800 – 500 – 400 – 333 – 250 – 200 – 133 – 100 – 80
MERCURY BICHLORIDE
STRYCHNINE
PILOCARPIN
CAFFEIN
SODIUM SALICYLATE
PHYSOSTIGMIN
TARTARIC ACID
ALCOHOL

TABLE II.—EFFECT OF TEMPERATURE ON GAS FORMATION.



had all been forced out of the upright tube. By this means no gas escaped into the air, and the yeast cells were cut off from atmospheric influences.

Results. These are given in the accompanying diagram (Table I.). The strength of the solution of the drug in the glucose-yeast mixture is indicated at the top of the columns. Increase of gas formation is indicated by rise of the action curve above the horizontal line, decrease of gas formation by depression below the line. It will be seen that no reliable stimulant was discovered. Alcohol gave curious results, sometimes having no effect, twice increasing gas formation, but generally decreasing it. The apparent stimulation in two cases may possibly have been due to some error in manipulation. Bichloride of mercury, 1 : 500,000, which is said to have a decided stimulant action on yeast, had but slight action at temperatures above 30° C.

The effect of different temperatures was ascertained in another series of experiments. A temperature intermediate between 35° and 40° C. proved to be the optimum temperature (see dotted curves, Table II.) for fermentation in undrugged tubes. The action of the drugs given in Table I. was the same in quality at 30° C. as at 35° to 40° C., except that bichloride of mercury showed marked stimulant action at 30° C. and very little at higher temperatures. (See Table II.)

All of these drugs were such as either have been reported to stimulate yeast activity or were considered as promising because of known stimulant action on cells of the animal organism.

V. The Antagonism of Heat and Strychnine on Yeast.

The search for a reliable stimulant proving fruitless, a study was made of the effect of heat as a physical stimulant, and of the antagonistic action of strychnine in preventing the stimulation by elevation of temperature.

The results of two series of experiments are shown in Table III. It will be noticed that the average percentage of gas production under the influence of strychnine in the two series at 35°, 40°, and 45° C. range from 75 per cent. to 81 per cent. of the glucose for the thirty-minute period of growth, and from 79 per cent. to 86 per cent. for the forty-five-minute period, indicating practically the same degree of strychnine action for all three temperatures.

At 30° and 37° C., however, the depressing action of the strychnine is very much more pronounced for both periods of growth than at any other temperatures (58 to 73 per cent.); therefore we cannot be dealing with a case of pure antagonism, for if the effects of strychnine and heat were strictly antidotal the counteraction should be quantitatively the same at successive temperatures, or should, at least, vary in a constant

direction, as it does in the case of time. Table IV. illustrates this point, namely, that the increased amount of gas formed in the forty-five-minute periods as compared with that formed in the corresponding thirty-minute periods would make a fairly smooth curve for both strychnine and glucose.

TABLE III.—EFFECT OF TEMPERATURE ON GAS FORMATION.

	Temperature, amount and percentage of gas.										
	30°		35°		35°-37°		40°		45°		
	C.c.	o/o	C.c.	o/o	C.c.	o/o	C.c.	o/o	C.c.	o/o	
Pure glucose	1.2	100	1.4	100	2.0	100	2.2	100	2.7	100	1st series.
30 min. growth	0.6	100	1.4	100	3.0	100	2.5	100	2.9	100	2d "
Strychnine 1 : 500	0.7	58	1.1	78	1.3	65	1.6	72	2.0	74	1st "
30 min. growth	0.4	66	1.2	85	1.9	63	2.0	80	2.2	76	2d "
Pure glucose	2.1	100	2.8	100	4.0	100	3.4	100	4.0	100	1st series.
45 min. growth	1.4	100	2.7	100	4.5	100	4.9	100	4.0	100	2d "
Strychnine 1 : 500	1.3	61	2.0	87	2.35	59	3.0	88	3.1	77	1st "
45 min. growth	1.0	71	2.2	81	3.3	73	3.4	85	3.3	82	2d "

TABLE IV.—EFFECT OF TIME ON GAS FORMATION.

	Temperature, amount and percentage of increase.										
	30°		35°		35°-37°		40°		45°		
	C.c.	o/o	C.c.	o/o	C.c.	o/o	C.c.	o/o	C.c.	o/o	
Pure glucose	0.9	76	0.9	57	2.0	100	1.2	54	1.3	48	1st series.
	0.8	133	1.3	92	1.5	50	1.5	60	1.1	38	2d "
Average	0.85	105	1.05	75	1.75	75	1.35	57	1.2	43	
Strychnine	0.6	84	0.9	81	1.0	80	1.4	87	1.1	55	1st series.
1 : 500	0.6	150	1.0	83	1.4	73	1.4	70	1.1	50	2d "
Average	0.6	117	0.95	82	1.2	77	1.4	78	1.1	53	

In regard to the effect of time, it is to be noted that the increase in the absolute quantity of gas is much more constant in the two series of experiments than is the increase of the percentage of gas.

VI. Conclusions.

1. Strychnine does not seem to affect the pulse when given simultaneously with alcohol.

2. In some cases (Experiments 1 and 3) strychnine seems to counteract in part the depressing effect of acute alcoholic poisoning on the respiration, and thus prolong life. The apparent exception (Experiment 2) is doubtless explained by the poor physical condition of the cat receiving strychnine and by the small dose.

3. Strychnine does not seem to interfere materially with the narcosis from acute poisoning with alcohol, but, apparently, does delay the onset of paralytic symptoms.

4. In subacute alcoholic poisoning (Experiment 4) strychnine seems to lessen the narcosis and paresis in the earliest stages, but in the later stages to increase the depression. However, a general conclusion is hardly justified, since only one control experiment was made.

5. Although in no case was the strychnine competent to completely remove the effects of the large doses of alcohol which were employed, yet it may be considered probable that appropriate doses of strychnine (fairly strong therapeutic doses) would prove useful in the treatment of poisoning from even lethal doses of alcohol.

6. No action on the nerve cells by either alcohol or strychnine was demonstrable histologically.

7. Many drugs depress the activity of yeast cells, but no reliable stimulant was found; therefore the antagonism of drugs in their action on these cells could not be studied.

8. Heat was found to be a reliable stimulant up to 45° C., but strychnine as an antidote to heat did not give uniform results at the successive temperatures, so that the antagonism is not a simple one.

BLOOD CHANGES IN DEMENTIA PARALYTICA.

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The blood of patients suffering from dementia paralytica has been the subject of microscopic study by many observers during the past fifty years, but none have made regular and systematic examinations extending over a considerable portion of the course of the disease. Believing that such a study, so conducted as to eliminate all known physiological changes, might throw further light upon the nature of this

important disease, this work was begun at the suggestion of Dr. August Hoch in the spring of 1901. The present is a preliminary report upon eleven cases.

HISTORICAL. The earliest known studies of the blood of paretics were made by Erlenmeyer and Hittorf in 1846 and 1847; Michale, 1848; Sutherland, 1873, and Voisin, 1879; but as their studies were made with instruments which would not give results comparable with our own, they are not taken into consideration.

Macphail,[1] in his study of fifteen cases of paresis, in which he laid special stress upon the blood state in different stages of the disease, ascertained that the hæmoglobin and erythrocytes were relatively low in the first stage, increased slightly during the quiescent period, and diminished greatly during the final stage, but showing, as a whole, a qualitative and quantitative diminution which runs parallel to the progress of the disease; also, that the leukocytes increased proportionately toward the end of the disease, and, finally, that states of excitement seemed to have an especially great influence upon the condition of the blood.

Thompson, as quoted by Macphail, in the examination of five typical cases of paresis in the stage of onset, the demented and the paralytic stages, found that within the first six months the hæmoglobin averaged 66.2 per cent., and the proportion of the white and red cells to be 1 : 308; six to fifteen months, hæmoglobin, 70 per cent., and whites and reds 1 : 176; and toward the end of the disease hæmoglobin 60.6 per cent., and proportion of whites and reds to 1 : 124.

The conclusions of Lewis, cited by Capps, were similar to those of Thompson.

Smyth,[2] in the study of forty cases of paresis in which the duration of the disease varied from the second to the thirty-third month, discovered that there was a diminution of hæmoglobin, except during periods of great exaltation, and a marked falling off in the number of red cells.

Winkler,[3] in four cases of paresis, three of whom were moderately nourished and one well nourished, found the hæmoglobin diminished as well as the number of red blood corpuscles. In one case they were high. They always diminished as the disease approached its termination. The changes of the blood were parallel with the loss of weight. In the stages of excitement the hæmoglobin and red blood corpuscles, both diminished at the onset, remained stationary in the period of quiescence and fell rapidly in the last stage. The body-weight presented a similar change, *i. e.*, in the stage of quiescence it remained the same or increased slightly, and in the end stages fell rapidly.

[1] Journal of Mental Science, 1884, p. 378. [2] Ibid., 1890, p. 504.
[3] Ueber Blutuntersuchungen bei Geisteskranken, Inaug. Dissert., Bonn, 1891, pp. 5–39.

Paralytic attacks had a bad effect upon the blood and produced a loss of weight.

Kryspiakiewicz[1] examined fifteen cases of paresis, mostly progressive cases and some during the terminal state and when suffering from acute decubitus. While his observations in general agree with those of Smyth, he also frequently found poikilocytosis, and a larger number of megalocytes and a smaller number of microcytes than is normally present.

Roncoroni,[2] in his study of fifteen paretics, in which he paid special attention to the eosinophiles, found that they were sometimes increased, sometimes diminished, but rarely normal, and that in paretic excitement there was regularly an increase, which in one case reached 25 per cent.

Burton, as cited by Somers, found in four cases of paresis a diminution of the leucocytes and of the hæmoglobin.

Somers,[3] in the examination of five cases of paresis, discovered a falling off of the erythrocytes and a slight increase of the leucocytes (8800), and a decline of the hæmoglobin (74.2).

Capps[4] in nineteen paretics found a more or less striking diminution of hæmoglobin (70 to 90 per cent.), but a steady increase was noted, dating from the admission to the hospital, which, by the author, was believed to be due to the improved hygiene and nutrition. In only four cases did the erythrocytes reach 5,000,000. There was present in the majority of cases a moderate leukocytosis, yet no conclusion could be drawn as to the relationship between the different stages of the disease and the degree of leukocytosis. He, however, failed to find a leukocytosis in two cases examined within four months of the onset, while one case of the same duration, but of rapid progress, did exhibit leukocytosis. In studying the variety of leukocytes, he found that the small lymphocytes were less numerous than normally, and the large lymphocytes were slightly increased, but sometimes three times the normal amount. The polymorphonuclear variety was slightly increased in fourteen of the nineteen cases, but in only one instance above 78.8 per cent.

Of rather more importance was his observations in reference to the blood changes at the time of a paralytic attack. Shortly preceding paralytic attacks, there was an increase of the erythrocytes and hæmeglobin, and shortly following them a very transitory but pronounced leukocytosis. The erythrocytes and hæmoglobin fell a few hours later. The intensity of the leukocytosis depended upon the severity and the duration of the attack.

[1] Wien. med. Wochenschrift, 1892, No. 25.
[2] Archiv di Psichiat. Scienze, 1894, vol. xv., fasc. 111, p. 293.
[3] New York State Hospital Bulletins, January, 1896.
[4] The American Journal of the Medical Sciences, 1897.

Jeliffe,[1] in his observations, which consisted of one examination in each of seventeen cases, ascertained that the hæmoglobin was reduced in nearly all cases, that the erythrocytes were comparatively high, the number being increased in fourteen of the seventeen cases, and in eight of these amounting to more than 6,000,000. The leukocytes were reduced in seven cases, and in only three cases was a leukocytosis recorded, and accompanied in each case a "general exalted condition." His observations on the differential count, in general, accords with those of Capps, except that the author calls attention to the complete absence of eosinophiles in some cases.

CASE I.—The patient developed his psychosis at the age of forty years. He was known to have been intemperate. The character of the disease, during the first twelve months, was one of simple progressive dementia, which did not necessitate confinement. He then, rather suddenly, exhibited great motor restlessness with violence, expressed many expansive delusions of a religious nature and some hallucinations, and consciousness became greatly clouded. He was admitted to the hospital two weeks later. The condition of paretic excitement continued without abatement for about one month, when it gradually disappeared, leaving the patient in a condition of profound dementia, with greatly impaired memory, clouded consciousness, paralysis of thought and volition, and emotional indifference. Extremely expansive and Nihilistic delusions were alternately expressed, while his conduct was characterized by occasional outbreaks of irritability and violence, but otherwise he was orderly. Physically, he presented fine muscular tremor, considerable inco-ordination, faulty articulation, exaggerated deep reflexes, and unequal pupils, which responded to light within narrow limits.

The patient was in this condition at the time the blood examinations were begun, and continued without appreciable change until the twenty-fourth month, when he gradually became noisy and extremely filthy, but did not show any other evidence of increased psychomotor activity. Meanwhile, he had improved greatly in nutrition. In the twenty-sixth month, following a rather rapid fall in nutrition, he suddenly developed an apoplectic attack, with left hemiplegia, from which he recovered in five days. He then, for the first time, expressed delusions of poisoning, and persistently refused food, with consequent rapid emaciation, and death twenty-two days later, preceded by somnolence and, finally, stupor. The paralytic attack was followed in twenty-four hours by a high temperature (104° F.) which subsided on the third day, but from that time until death there was a pretty constant daily variation of temperature, extending from 96.6° F. to 100° F. There was no evidence of an acute inflammatory process which might account for a leukocytosis. The weight fell rapidly during the final fourteen weeks, dropping from 157 to 85 pounds.

A post-mortem examination was not made.

The study of the blood in this case, which comprised sixty-one weekly examinations, began just after the subsidence of the paretic excitement. During the first month both the hæmoglobin, the ery-

[1] New York State Hospital Bulletins, July, 1897.

throcytes, and leukocytes averaged below normal, but following this and during the entire quiescent period, except for four weeks preceding the paralytic attack, and when the nutrition was beginning to fall, the hæmoglobin averaged 85 per cent., thence the hæmoglobin fell to an average of 74 per cent., until it began to rise nine days before death, and two days before death reached 92 per cent.

The erythrocytes rose to normal and remained within normal limits until the fall in nutrition, when they fell to below normal, and remained there until the nine days previous to the paralytic attack, when they rose to normal and gradually increased until they reached 6,386,000 two days before death.

The leukocytes following the first four weeks remained high normal for two and one-half months, when they fell to low normal and at times below 5000, where they remained for ten weeks; then high normal for four weeks, followed for sixteen weeks by a count varying between 8600 and 6000, with one exception, when for a week they rose to 9500. Then, one week previous to the fall of nutrition, when both the percentage of hæmoglobin and number of erythrocytes diminished, the leukocytes fell to 5000 and remained subnormal, with one exception (6800), until the terminal rise which began sixteen days before the paralytic attack, but did not become a distinct leukocytosis until the ninth day following it. The leukocytosis reached its height seven days previous to death, and fell on the last count to 13,5000. Among the leukocytes the polymorphonuclear variety predominated throughout, the percentage of which varied from 5 to 26 per cent. above the normal; upon only one occasion did it approach normal, and then it was 71.8 per cent. The greatest increase appeared during the final leukocytosis, when the percentage remained above 92 per cent. during the last four counts.

Case II.—This patient gave the first evidence of his disease at the age of forty-two years. It was of gradual onset, with a loss of interest in his work and a lack of endurance. At times he was also forgetful. He, however, continued at work for seven months, at which time he rather suddenly developed many changeable delusions of grandeur, with a feeling of well-being and an increased activity. One month later, when admitted to the hospital, he showed a defect of memory for both recent and remote events, a pronounced feeling of well-being, some pressure of activity, together with the most extremely expansive delusions, insomnia, anorexia, and loss of weight. Physically, there were contracted pupils which were irresponsive to light, general muscular tremor, faulty articulation, some ataxia of the lower extremities, absence of knee-jerks, and a lack of muscular tone. In the ninth month he developed a condition of paretic excitement during which the first examination of the blood was made. After a duration of two months this condition suddenly disappeared, leaving the patient in a condition of deeper dementia. He continued mildly elated but orderly in conduct. After an intermission of five weeks the condition of great excitement returned and continued for one month, when it again vanished. He lost sixteen pounds in weight, and at the end showed great muscular weakness. At this time the feeling of well-being was replaced by one of despondency and fear of death, and all delusions vanished. While he was quite orderly in conduct, took some interest in his surroundings, aided in ward duties, and spent much time in reading, he

had lost all power of endurance, and usually became so fatigued by afternoon that it was necessary for him to go to bed; at the same time speech became confused. The condition of muscular paresis gradually progressed, and terminated fatally in an attack of syncope four months later, the total duration of the disease being nineteen months.

The temperature during the last four months occasionally dropped to 96° F., and even 95° F., and rose to 100° F., and on a few occasions to 102° F. and 103° F. without any apparent cause. During the two weeks preceding the paralytic attack it was mostly subnormal. Ten days before death it rose to 100.6° F.; thence there was a daily rise and fall, varying between 100.8° F. and 97° F., reaching 101.8° F. on the day of death. There were no objective signs of an acute inflammation process. The weight fell gradually from the eleventh month, when it was 139 pounds, to 79 pounds at the time of death. An autopsy was refused in this case.

The blood analysis began during the height of his first paretic excitement. The first two examinations, which were made at an interval of twenty six days, showed the hæmoglobin to have risen from 73 to 100 per cent., and the leukocytes from 6500 to 10,300, while the erythrocytes remained at low normal. The remaining counts were made bi-weekly until the last two months, when they were made weekly. In the remission of five weeks the hæmoglobin remained between 77 and 83 per cent., the erythrocytes rose from low to high normal, while the leukocytes went up to 14,000 and then fell to 7800. In the period of excitement which followed this for two months, but which was not as intense, though it led to great physical weakness and the loss of nearly sixteen pounds in weight, the hæmoglobin varied between 76 and 102 per cent.; the erythrocytes remained normal and high normal, and rose at one time to 5,800,000, and there was a leukocytosis, except for one week, when the leukocytes fell to 8700. During the quiescent period of four months which followed the hæmoglobin varied from 62 to 89 per cent., but averaged 76 per cent.; the erythrocytes remained normal and high normal, except on two occasions, when they fell to 4,000,000, and 4,500,000; the leukocytes varied considerably, twice falling to nearly 6000 and once below, and three times showing a moderate leukocytosis; otherwise they were about normal. The examination of the blood on the day of the collapse showed the hæmoglobin at 67 per cent., the erythrocytes at 4,888,000, and the leukocytes at 8400. Six days later, while the patient continued to fail and at the time was in a semicomatose condition, the hæmoglobin rose to 82 per cent., the erythrocytes to 5,982,000, and the leukocytes to 16,000. Death occurred sixty hours later.

The differential count showed, throughout the whole psychosis, a great increase in the percentage of polymorphonuclear leukocytes, which reached at the last two counts 90 and 86.4 per cent.

CASE III.—This case is not cited in full because of the limited study of the blood, which comprised two examinations, on the twelfth and seventh days before death.

The patient first gave evidence of the psychosis at fifty-four years of age. There was some insane collateral heredity, but otherwise no etiological factors could be ascertained. The disease was of gradual onset, and the symptoms were those characteristic of the demented form until one week previous to his commitment in the twelfth month, when

he rapidly developed symptoms characteristic of the agitated form of the disease. This condition of intense excitement continued until he fell into a semicomatose state seven days before death, which gradually deepened, being accompanied by a dysenteric condition. The physical signs of the disease were well advanced at the time of his admission. The patient was much emaciated, which condition rapidly increased until death. There was no autopsy in this case.

In the two blood examinations the percentage of hæmoglobin was at first 90 per cent., but then fell to 65 per cent. The erythrocytes were normal, and then fell below normal; the leukocytes showed a leukocytosis (10,000), which advanced to 14,100, in which there was an increased percentage of polymorphonuclear leukocytes (84 and 86 per cent.).

Case IV.—The exact date of the onset of the psychosis and the character of its early symptoms are unknown. At the time of her admission she was thirty-four years of age, and the disease had already reached the stage of profound dementia, with complete clouding of consciousness, greatly impaired memory, emotional deterioration and a considerable emotional irritability, pronounced limitation in the store of ideas, considerable incoherence, some increased psychomotor activity, and complete inability to care for herself. Physically she presented Argyll-Robertson pupils; great ataxia, which necessitated confinement in bed; faulty speech, pronounced tremor of hand and of facial muscles, exaggeration of deep reflexes, and considerable emaciation. Two months previous to her commitment she had a series of epileptiform attacks.

At the time of the first blood examination, which was made thirteen days after admission, the patient was still showing some psychomotor activity, confined mostly to a purposeless fumbling with her clothing, sometimes tearing or removing it, and incessant talking in a loud voice, but this gradually disappeared by the end of the first month of her residence.

At this time there suddenly developed a paralysis of the left arm, unaccompanied by other phenomena. From this time the activity began to diminish. In the fourth month her mind had become a complete blank, acute decubitus appeared, and the terminal phalanges of the paralyzed left hand sloughed off. From this time paresis of all the muscles became more marked, acute decubitus advanced, and she died three months later, at no time showing a rise of temperature. The weight could not be taken in this case. Post-mortem examination corroborated the diagnosis.

The examinations of the blood were made bi-monthly in this case, and show, in reference to the percentage of hæmoglobin, that it averaged low, especially during the last month of the disease (68 per cent.). Previous to this it reached 90 per cent. only on two occasions. The estimation of the erythrocytes showed a normal and high normal count, except for the first and next to the last examinations, when it fell to 4,200,000. During the second and third months previous to death it varied between 5,150,000 and 5,666,000, but during the terminal month it fell below 5,000,000, was lowest thirteen days before death, and then rose to about 4,700,000 four hours previous to her death. The leukocytes remained below normal during the first three months, except on two occasions, when there was a very moderate leukocytosis

(9733 and 10,666). Thence for one and one-half months it was high normal, and thence for one week there appeared a leukocytosis of 14,000. It then dropped to normal and low normal, except on the twenty-seventh day before death and four hours before death, when it reached 10,100 in the former and 14,600 in the latter. In the differential count the polymorphonuclear leukocytes were constantly above normal, and in the final leukocytosis reached 94.2 per cent.

CASE V.—This patient developed his psychosis at the age of thirty-five years. It was of gradual onset and characterized by a progressive deterioration in memory and judgment. Within a month he began to express numerous grandiose delusions, and showed considerable increase in activity. Two weeks previous to his admission to the hospital, in the twelfth month of the disease, he suffered from a series of epileptiform convulsions, followed by transitory paresis in the left arm and mentally by great clouding of consciousness and extreme activity, simulating the occupation delirium of senile dementia. This condition still persisted at the time of his admission. He was emaciated, insomnia was marked, the deep reflexes were abolished, the pupils did not react to light, and ataxia was marked. Dementia was profound.

At the time of the first blood examination, in the fourteenth month of the disease, the restlessness had somewhat subsided, but deterioration had advanced and emaciation had become still more prominent. He was, however, very loquacious. In the fifteenth month the activity began gradually to increase, and the patient became destructive, filthy, and very noisy. By the third week the excitement had become extreme, and continued so for one week, when the patient developed epileptiform attacks, which assumed the form of an epileptic status and lasted for twenty-four hours, followed by a semicomatose state, which terminated fatally eight days later. During his five months' residence in the hospital the patient gradually fell in weight from 123 pounds to about 85 pounds. The temperature was not taken during his final illness, but apparently was normal. An autopsy revealed the characteristic lesions of paresis.

In studying the condition of the blood, which was examined weekly until the final ten days, when four counts were made, we find that the hæmoglobin did not show any great variation. During the period in which the motor excitement had subsided, it rose to 90 per cent. on three occasions, but from that time on it remained pretty constantly about 85 per cent., with one exception, which was the day following the epileptic status, and then it fell to 76 per cent. The erythrocytes remained about normal until the final excitement, when they gradually rose until the day following the convulsions, then fell to normal, but four days later, which was three days previous to death, they had reached 6,333,000. The leukocytes remained below normal until the appearance of the great excitement preceding the convulsions, when a leukocytosis appeared. This reached 17,200 the day following the convulsion, but had dropped to 14,200 three days before death. We find among the different forms of leukocytes present that the polymorphonuclear variety was always above 79 per cent., and during the terminal leukocytosis reached 93.4 per cent.

CASE VI.—The patient developed her psychosis at the age of forty-one years. The onset was gradual and characterized by despondency, delusions of self-accusation and fear, but further than this the nature

of her psychosis was unknown until her admission to the hospital one year later. At this time she was profoundly despondent, showing great apprehension and expressing fear of death. She was greatly agitated and lamented loudly. In fact, the clinical picture was that of the so-called "agitated melancholia." Physically she presented marked emaciation, anorexia, and constipation, but none of the characteristic physical symptoms of dementia paralytica. In the fifteenth month of the disease she began to improve rapidly, and in the course of one and one-half months had apparently recovered, in this time having gained ten pounds in weight.

During the succeeding twenty-five months the patient seemed quite normal, except that she exhibited a greater tendency to indulge in alcoholic excesses.

The disease gradually reappeared at the age of forty-three years. She began to neglect her household duties and her own personal appearance, would serve her meals uncooked, stole money from her husband and spent it for liquor, attempted to travel away from home without money, and at times was threatening. Upon admission to the hospital three months from the onset it was found that she had already greatly de iorated, especially in memory and judgment. Many absurd and e tren y grandiose delusions were expressed. There was marked emoti al terioration, while her volitional condition exhibited stupor, relieved at times by some pressure of activity, volubility, and a feeling of well-being, with impulsive violence. Physically she presented an absence of tendon reflexes, pupils that were unequal and refused to react to light, faulty articulation, considerable muscular tremor, some ataxia, and general lack of muscular tone. In the fifth and sixth months dementia had gradually advanced, while the stupor and occasional excitement had disappeared. In the seventh month stupor, with negativism, appeared. She refused food, resisted everything, and displayed no voluntary activy. The stupor increased, the loss of weight and general paresis became marked, and death occurred in the sixth week of the stupor. The temperature was slightly subnormal during the last week, and at the time of the final blood examination on the day of the death was 93.4° F. in the axilla. A permission for a post-mortem examination could not be secured.

The blood examinations in this case were confined to the period of final stupor. The first examination was made in the second week of the stupor, at a time when the state had not become very profound, and the last about ten hours before death, the counts being made at weekly intervals.

In the five examinations there was a rapid diminution of the percentage of the hæmoglobin from 85 to 60 per cent. for the first four, and then a final rise to 65 per cent.; the same change occurred in the count of the erythrocytes, which dropped from 5,488,000 to 3,711,000 and in the final week rose to 4,484,000. On the other hand, the leukocytes were below normal for the first two weeks and then showed an increasing leukocytosis, which reached 25,000 the day of her death. Throughout the whole period the increase in the number of leukocytes was largely represented by an increase of the polymorphonuclear leukocytes, which never fell below 82 per cent.

Case VII.—In this case the disease appeared gradually at fifty-four years of age. At first it was noticed that the patient began to drink to

excess. He then became drowsy and heavy and slept a great deal of the time. Details of his work were overlooked, and he showed great irritability. Morally he lost his sense of propriety and was occasionally obscene. Under the influence of rest and total abstinence he gradually improved from the sixth to ninth month, and from the ninth to seventeenth months seemed "nearly well" and "perfectly natural."

In the seventeenth month, following exposure and overwork on the farm, he began to express delusions of grandeur and show some psychomotor restlessness, which with great irritability made his confinement in an institution necessary seven weeks later. At this time he presented some time disorientation; slight incoherence in his train of thought; impairment of memory and many changing delusions of grandeur of the most florid type, involving every sphere of life. There was also a pronounced feeling of well-being, with considerable emotional irritability and lack of moral feelings. His pressure of activity was confined mostly to an intense busyness, writing important letters, sending telegrams, etc. Physically there were exaggerated tendon reflexes, Argyll-Robertson pupils; muscular tremor, especially of facial muscles; inco-ordination and greatly impaired articulation.

This condition of excitement greatly increased, and at the time of his first blood examination, one month later, was extreme. His sleep was greatly disturbed and he had lost nineteen pounds in weight. The excitement began to abate in the second and third months, so that it was possible to keep him clothed. Suddenly the patient developed a stuporous condition over night. In the morning his consciousness was found to be greatly clouded, memory was much impaired, he was silent, and only fragments of his former grandiose ideas could be obtained by direct questions; emotionally the elation had been replaced by indifference, and his activity had mostly disappeared. Physically muscular exhaustion with increased tremor and inco-ordination had appeared, the countenance had become ashen and sunken. This stupor increased and death occurred thirty-six hours later, in the twenty-third month of the disease. During the week previous to the appearance of the stupor his weight fell eight pounds. The temperature was slightly subnormal during the stupor.

Consent for post-mortem examination could not be obtained, and the diagnosis could not be verified.

The examination of the blood, which consisted of bi-weekly examinations, shows the hæmoglobin to have remained subnormal until the day previous to the appearance of the stupor, when it rose to 105 per cent. The erythrocytes were subnormal at the time of the first examination, but had increased 1,000,000 by the second examination, then they steadily fell with the slight abatement of the excitement until the day before the stupor, when with the hæmoglobin they rose to 5,088,000. The leukocytes were subnormal until the last examination, when they rose over 3000, producing a slight leukocytosis. In this elevation the polymorphonuclear leukocytes jumped up about 20 per cent., with a corresponding drop in the small lymphocytes, which had been 37.2 per cent. and 39 per cent., but with this exception the character of the leukocytes had been normal.

This case is of greatest interest because it shows the tendency to an abrupt rise in all three elements of the blood one day preceding the appearance of the fatal stupor.

CASE VIII.—At forty-six years of age this patient began to "fail in health," to lose in weight, and suffer from malaise; but it was not until seven months later that mental symptoms appeared, at which time he neglected his work, became loquacious and displayed a moderate feeling of well-being. A few somatic delusions were expressed, such as that he had revolving wheels in his head, which he feared would wear through the cranium and cause death, and his memory for recent events was impaired. He was admitted to the hospital three months later, when he was partially disoriented, and showed marked impairment of memory, some feeling of well-being, and motor restlessness. Physically he presented ataxia, general muscular tremor, faulty speech, Argyll-Robertson pupils, exaggerated reflexes, and impaired nutrition. In the course of two months the restlessness and loquacity disappeared, consciousness cleared, somatic delusions vanished, and nutrition improved. Constant hallucinations of hearing, however, appeared, with delusions of infidelity and of reference, which made him despondent. It was at this time that the blood examinations were begun. He was orderly in conduct and an excellent helper in the ward.

His mental condition remained unchanged during the succeeding six months. The hallucinations of hearing continued and caused him much anxiety in reference to his wife. During the latter part of this period he suffered from insomnia and terrifying dreams and steadily lost in weight. The physical symptoms had not advanced. Without warning he suddenly became greatly agitated, reacted to numerous hallucinations of hearing, assaulted fellow-patients and attendants, resented his confinement, removed his clothing without purpose, and exhibited great motor restlessness. Consciousness remained clear. Food was refused and sleep completely abolished. At the end of the fourteenth day the patient became comatose and died forty-eight hours later.

During the quiescent period his weight gradually fell fourteen pounds, and during the final period of excitement dropped thirty-six pounds. The temperature was not taken, but from all external indications was normal.

A study of the tabulated record of the blood examinations shows that the erythrocytes throughout the period of quiescence, extending from the twelfth to the eighteenth month, with few exceptions, remained constantly normal and high normal. During the eight weeks previous to the terminal excitement there had been a gradual rise for seven weeks and then an abrupt drop of 900,000. In this same period the hæmoglobin at first averaged about 89 per cent., when it fell and averaged during the last thirteen weeks about 82 per cent. The leukocytes at first continued about normal, but during the last thirteen weeks of this period fell to low normal, and sometimes even to 5000. The week previous to the exacerbation a leukocytosis appeared. In the differential estimation of the leukocytes we find that the polymorphonuclear leukocytes were always in excess of the normal percentage by ten to fifteen points, while the small lymphocytes presented a continuous lymphocythæmia. The large lymphocytes were continually below normal during the latter part of this period.

The final period of the disease, that of the excitement, presents a marked change. In the first place, there was a progressive increase in the number of the erythrocytes after the second week, reaching, eight

hours before death, 7,551,000; the hæmoglobin showed a corresponding rise to 110 per cent. The leukocytes from the week preceding the exacerbation began to increase, and in the final count reached 27,000. The increase occurred entirely in the polymorphonuclear variety, which at the end averaged 91.6 per cent.

The post-mortem observations in the case verified the diagnosis of general paresis, and failed to reveal any cause for the leukocytosis.

CASE IX.—The onset of the disease occurred at forty-three years, six months previous to the patient's admission to the hospital. He began to drink to greater excess, and when under its influence became violent. His work was abandoned while he spent his time loafing about the neighborhood. He presented a feeling of well-being, and in a short time expansive delusions appeared. He was shiftless and careless, and upon two occasions set the house on fire with ashes from his pipe, but on neither occasion made any effort to extinguish the flames. At the time of his admission he was still expansive and had a feeling of well-being. Deterioration was evident from his impaired memory and judgment and lack of emotional reaction. There was no increased activity, and consciousness was clear. Physically the pupils were unequal and irresponsive to light, tendon reflexes were absent, and there was faulty speech, general muscular tremor, moderate ataxia, and greatly disturbed speech. From the eighth to tenth months the expansiveness and feeling of well-being gradually disappeared, while the irritability increased, leading to occasional outbursts of passion with destructiveness. In the tenth month he suffered from his first epileptiform attack, preceded for a couple of days by lightning pains in his legs and followed by great restlessness and violent aggressiveness. During the following five months periods of composure with insight and fear of impending death alternated with periods of restlessness, irritability, and threatening and violent behavior. In the thirteenth month the second paralytic seizure occurred, preceded by five days of excitement and followed by composure. During the sixteenth to twenty-first months he had a partial remission, with an improvement in memory, emotional attitude, and conduct.

The first blood examination was made during this remission, but the second examination was not made until the termination of the remission, with a stupor in the twenty-first month. The examination was made on the second day of the stupor, when the patient was completely clouded, experiencing hallucinations of sight, incoherenec of thought, and slight restlessness. On the same day an epileptoid spasm of the clonic form appeared, involving only the right upper and lower limbs, followed by hemiparesis of this side lasting some days. The stupor disappeared in the course of five days, but mental deterioration had advanced, and the patient presented greater languor, indifference, and irritability. For the three succeeding months he showed considerable gradual improvement. Dazedness again suddenly appeared in the twenty-fourth month, with evident hemiparesis of the left side, from which he never fully recovered He remained semistuporous for two months, was thoroughly disoriented, and memory for all of the events of his life was greatly impaired. During this time he suffered from an epileptiform attack involving the left side and followed by a partial paralysis of this side. The convulsive twitchings lasted several days. The quiescent stage followed from the twenty-sixth to the twenty-

ninth months. Another and exactly similar seizure to the above, involving the left side and producing paresis, occurred in the twenty-ninth month. The twitching continued for four days. Two weeks later a slight clonic seizure occurred involving the left side. Three days following this the patient developed a comatose state, with twitching of the right hand, weakened pulse, and febrile temperature, appearance of bronchopneumonia on the ninth day, and death on the eleventh day.

The post-mortem examination disclosed the anatomical lesions characteristic of dementia paralytica and also bronchopneumonia.

The study of the blood in this case began during the remission between the sixteenth and twenty-first months. At that time there was a moderate leukocytosis and a high erythrocyte count. The second examination was made on the second day of the stupor which followed the remission, and from this time examinations were made weekly until death. Six hours previous to the second examination the patient developed an epileptoid attack which lasted ten hours. Throughout this stupor the erythrocytes remained a high normal, with hæmoglobin varying between 85 and 95 per cent.; the leukocytes showed a leukocytosis 11,000 to 20,000, which reached its height in the second week. During the following ten weeks, while dementia was gradually progressing, the hæmoglobin remained high, for three weeks being above 100 per cent., but during the last two weeks falling below 75 per cent. The erythrocytes continued high, upon two occasions passing the 6,000,000 mark. The leukocytes fell abruptly to below normal, then rose slightly in the third, fourth, fifth, and sixth weeks, maintaining a slight leukocytosis, and again in the eighth week reached 10,300. In the tenth week, on the day when the condition of dazedness suddenly appeared accompanied by hemiparesis, the leukocytes reached only 9500.

From this time until three weeks previous to death, while the mental condition did not change greatly, the progress of the disease was marked, however, by paralytic attacks. The hæmoglobin averaged 80 per cent., upon one occasion reaching 65 per cent., the erythrocytes remained about 5,000,000 until during the final eleven weeks, when they averaged about 4,700,000, except upon one occasion, when they rose to 5,546,000, and fell back again the next week without apparent reason. During the final comatose state of two weeks the erythrocytes fell to 4,131,000, and on the day before death to 3,600,000.

The leukocytes during the period from the twenty-third to twenty-ninth month were mostly below normal, except near paralytic attacks. The week following the attack in the twenty-third month they reached about 10,500. They were then subnormal until the next attack, which lasted three days. The count was made on the day following the onset and showed a leukocytosis which continued into the next week. Four and five weeks later a leukocytosis appeared without any evident change of the mental symptoms. Likewise five weeks later and also seven and eight weeks later a slight rise above normal occurred. The next rise occurred thirteen hours preceding an attack, and again three weeks later a moderate leukocytosis accompanied another attack. In the coma which followed this attack and led to death the leukocytosis was 13,700, and one week later, the day previous to death, 10,700. In the differential count we find that during the periods of leukocytosis

throughout the disease the polymorphonuclear leukocytes predominated in percentages varying from 60.6 to 90.4 per cent., but upon only two occasions being below 70 per cent. His weight charts show a gradual fall from the twenty-third month, and during the last two weeks a loss of over ten pounds.

His temperature at the time of the blood counts did not vary over a degree from normal, except during his final illness, when it remained subfebrile, except at the final count, when it was 105° F., ten hours after developing bronchopneumonia.

CASE X.—The onset of the psychosis was gradual at the age of thirty-five years, with a pronounced change of character, the patient becoming irritable, very forgetful, and at times dazed. Within a month of the onset he had a paralytic attack, and following this the memory was more impaired, and he seemed uneasy, and could not apply himself to his work. His memory and judgment had so far deteriorated by the tenth month that he was incapable of doing any work. At this time he began to express delusions of grandeur and to exhibit a feeling of well-being.

He was admitted to the institution in the twelfth month of the disease, with profound deterioration in both memory and judgment, clouded consciousness, extremely expansive delusions, and a marked feeling of well-being. He was busy in planning various grandiose business adventures, and had no thought or feeling for his family. Physically he presented an absence of knee-jerks, Argyll-Robertson pupils, inco-ordination of lower extremities, faulty articulation, general muscular tremor, absence of facial expression, and impaired nutrition.

During the first month after admission the patient showed some improvement, his consciousness became clear, the expansive delusions were less prominent. He became interested in his environment and was an excellent, energetic ward helper. Physically his state of nutrition improved greatly, and his weight rose seventeen pounds. There was no further change in his condition from the thirteenth to the twenty-third month. The blood examinations had been begun during the quiescent period.

In the twenty-third month the patient gradually developed a condition of stupor, he lost his former interest, stood about in one place unobservant, seemed unable to comprehend questions, and answered very slowly, giving evidence of difficulty of thought. All the delusions had disappeared and he expressed some insight into his condition. He was confined in bed. In seven days his stupor had deepened so that he did not respond at all to questions, and had to be fed by spoon. His weight continued to fall rapidly and his countenance became ashen. On the fourth day his temperature rose to 104° F., then fell to subnormal for two days, and from that time continued to show a slight afternoon rise to about 99.6° F. The stupor became more profound, and he died on the fourteenth day. In the two weeks his weight had fallen from 151 to 107 pounds.

In reviewing the blood charts of weekly counts which began during the quiescent stage at the seventeenth and one-half month of the disease we find that the hæmoglobin remained constantly low throughout this period. Upon three occasions it rose above 90 per cent., once to 93 per cent., and fell as low as 74 per cent.; its average, however, was 84 per cent. During the seventeenth and eighteenth months it varied

between 87 and 93 per cent., while during the final two months it varied between 88 and 74 per cent. During the period of stupor it fell at first to 65 per cent., and then rose gradually to 90 per cent. at the final count—four days before death.

The erythrocytes during the period of quiescence remained mostly normal, three times they rose above 5,500,000, and once to 5,871,000, until they fell with the hæmoglobin, and from that time until the final stupor remained below 5,000,000, once reaching 4,500,000. During the stupor they gradually rose from 4,500,000 to 6,500,000.

The leukocytes, similarly with the erythrocytes, remained about normal, with one exception, when they rose to and over 10,000, then fell and were subnormal, averaging about 5,000. During the first part of the stupor, while it was still not profound, they rose gradually to normal, and then passed into a state of leukocytosis.

In reference to the relation maintained by the different forms of leukocytes we find that the polymorphonuclear leukocytes were about normal until the appearance of the leukocytosis, when they rose to 80.4 and 86.2 per cent.

During the final stupor there was a pronounced lymphopenia, while the large lymphocytes remained at the same percentage.

The autopsy in this case substantiated the diagnosis of dementia paralytica.

Case XI.—This patient developed dementia paralytica at the age of thirty-six years, but did not come under our care until one and one-half years later.

At this time he presented as evidences of the disease an impairment of memory, some clouding of consciousness, emotional deterioration, and increased motor activity, and an extremely limited content of thought. Physically he presented a very pronounced choreiform condition, which simulated very closely advanced Huntington's chorea; also exaggerated deep reflexes; tremor of the muscles of the face, tongue, and hands, inco-ordination of the limbs and facial muscles, and a moderately defective speech. In reading there was an elision and an occasional translation of syllables. He was also poorly nourished.

The patient was in this same condition at the time the blood examinations were begun, which was in the twentieth month of the disease, one and one-half months after admission. His condition did not change until the latter part of the twenty-third month, when he would become dazed for a few hours at a time. While in this state he was completely clouded, and would fail to respond to the dinner call. In three weeks he gradually passed into a stuporous state. The duration of this stupor was from February 19th to April 14th, when he emerged from the condition during a night. The next morning he was active and interested, asked for work, and talked freely of his war experiences. There was no motor restlessness. His condition of deterioration had apparently not advanced during the stupor, while the choreiform condition had greatly improved and was now confined entirely to the muscles of the face.

A condition of stupor, similar in every respect to the former one, came over him suddenly on June 30th, ten weeks later. On the morning of the tenth day he seemed somewhat improved, as he voluntarily went to the bath-room; a few minutes later he fell in a convulsion and expired in three minutes.

The post-mortem examination in this case substantiated the diagnosis of dementia paralytica.

In this case the blood examinations were begun during a condition of moderate paretic excitement, which persisted until the gradual appearance of a stuporous state in the twenty-third month. During the first three months only four examinations were made. Following this for three months they were made weekly, and during the last two months bi-weekly. During the first three months the hæmoglobin varied between 70 and 95 per cent., the erythrocytes were normal, with one exception, when they fell to 4,511,000, and the leukocytes were low normal and subnormal. During the stupor of two months' duration the hæmoglobin varied from 65 to 85 per cent., the erythrocytes increased from subnormal to above normal, and then fell to normal; the leukocytes averaged low normal. In the period of two weeks' intermission the hæmoglobin varied from 68 to 80 per cent., the erythrocytes remained normal, and the leukocytes averaged normal. No blood count was made during the eleven days previous to the onset of the second stupor, and the final examination was made six days before death. This examination revealed a normal count, with the exception of the low hæmoglobin and the high percentage of the polymorphonuclear leukocytes (77.8 per cent.).

The clearly defined periods of stupor are not indicated by a definite blood change. The weight, on the other hand, shows a progressive drop from the time of the first examination to the time of death, a loss aggregating forty-four pounds.

TECHNIQUE. The blood has been drawn from the finger, preferably a middle finger, precautions being taken to avoid the application of friction and pressure. The hæmoglobin has been uniformly estimated with a Fleischl's hæmometer, attention being paid that all excess of blood is carefully wiped from the end of the capillary tube. The erythrocytes have been counted with a Thoma-Zeiss hæmocytometer, the same pipette being used for practically all of the work. In using Gower's solution, making a dilution of 1 : 200, an attempt has always been made to place the cover-slip over the Zappert counting chamber as rapidly as possible after placing the blood in the chamber. Two large squares in each of two drops and one in the third drop, preferably squares near the periphery, have been counted in making the estimation. Wherever there was great variation another drop has been counted, and the three counts nearest each other selected in making the aggregate.

In counting the leukocytes acetic acid solution, with a dilution of 1 : 20, has been uniformly employed. Three fields of four hundred squares each have been counted in each case, and if there was a great variation an additional field was counted.

As regards the personal equation, the greatest part of the work has been done by a single observer. The work was begun by Mr. Burr, laboratory technician, in the spring of 1901 (thirty counts), continued by Mr. Stone, medical interne (sixty counts), and completed by Mr.

Ward, technician, all of whom had had considerable experience in blood work. Besides this, parallel counts were made to determine the presence of any error due to personal equation.

In reference to the condition of the patient, every precaution was taken to have the work uniform. In most cases the examinations were made weekly, occasionally bi-weekly. They were made at the same time of day, either two hours after breakfast or an hour and one-half after a dinner, and on the same day of the week. All patients were on uniform diet.

In enumerating the different forms of leukocytes, five hundred cells were counted.

HÆMOGLOBIN. In interpreting the results of our observations the standards established by Reinert in his extended series of observations upon normal individuals have been followed. The results of Reinert have been confirmed in great part by Mr. Ward, who also made a series of twenty-four-hour counts upon normal individuals. In order to ascertain if daily pathological variations occurred in the paretic, a similar series of twenty-four-hour counts was made by him in one of the patients.

In all of the eleven cases the observations were necessarily confined to a period of the disease in which the disease process was already well established.

The hæmoglobin in all cases showed a moderate anæmia, which became more marked, but never profound (below 65 per cent.) as the disease advanced. In cases where the hæmoglobin was below 80 per cent. at the time of the first examination it did not subsequently vary much.

During the terminal state the average percentage of hæmoglobin in all but three of ten cases (IV., V., and X.) was from 3 to 20 per cent. higher than during the period just preceding. Of the three cases in which the rise in hæmoglobin was not coincident with the onset of the terminal state, there is in one a rise in the last four weeks from 65 to 70 per cent., in another during the last three weeks a rise from 65 to 90 per cent., and in the third case a rise in the last week (two counts) from 76 to 86 per cent. The only exception to the increase of the percentage of hæmoglobin in the terminal state is found in Case VI., in which the blood was examined only during this period. In this case there was a progressive drop in four weekly counts from 85 to 60 per cent.

In reference to the relationship between the condition of nutrition and the percentage of hæmoglobin, four of the eleven cases were well nourished throughout the period of examination until just preceding and during the terminal state, and seven were poorly nourished. The hæmoglobin in the well-nourished cases averaged only 4 per cent. higher than in the poorly nourished—78 and 82 per cent. In two of

the well-nourished cases the hæmoglobin reached 100 per cent., and plus three times in one, and once in another case and three times in one of the poorly nourished patients.

The hæmoglobin during the various paretic states of quiescence, of excitement and stupor, not terminal, present no constant change, characteristic either of different states in the same individual or of similar states in different individuals. There was no increase in the percentage of hæmoglobin during the quiescent period, when nutrition regularly improved.

Erythrocytes. The erythrocytes in eight cases in which the examinations extended over many months averaged normal in all, while in the two cases (III. and VI.) in which the examinations were made only during a short period previous to death the average was low normal, but in no case was there an average subnormal count. Occasionally the cells sank to low normal, but in only five instances did they fall to subnormal; in one case once, in one case twice, and in one case three times. In the last two of these cases it occurred at the very end of the disease.

In all cases the erythrocytes showed a tendency to sink during the period just previous to the terminal state, and then there occurred during the terminal state, with only one exception, a rise which is even more marked than that seen in the hæmoglobin during the same period. This rise varied from 5000 to 3,000,000, and in four cases became a polycythæmia. This rise was exactly coincident with the beginning of the terminal state in only five of the ten cases.

The various paretic states, exclusive of the terminal state, namely, those of excitement, of stupor and quiescence, failed to exhibit any change in the erythrocytes. In the five cases of paretic excitement the count averaged normal in all but one, which was subnormal. In the two cases with the greatest excitement, in one of which there were two periods of excitement, the count averaged normal in one case and in one period of the other, and low normal in the other period. In the individual cases the count during the period of excitement averaged the same in two cases and lower in one. In one of the two cases in which it was higher the excitement occurred early in the disease, when the erythrocytes are naturally higher.

Stupor occurred twice in each of two cases. In three of these four stuporous states the count averaged normal, and in the other subnormal. In the individual cases the erythrocytes averaged higher during the period of stupor in one case and lower in the other.

Periods of quiescence could be studied in eight cases, in one of which it occurred twice. In five of these periods the count averaged normal, in two low normal, in one high normal, and in one polycythæmia. In the individual cases the erythrocytes during the period of quiescence averaged about the same as during the other periods of the disease in

three cases, lower in one case, and higher in the fifth case. In the remaining three cases there were no other paretic states except the terminal with which to compare it.

As regards the relationship between the condition of nutrition and the number of erythrocytes, the gradual, though not marked diminution in the number of cells as the disease advanced corresponded with the gradual loss of weight, except in the terminal state, when there was a tremendous loss of weight, but a considerable increase in the number of cells. In the three well-nourished cases (I., VIII., and X.) the erythrocytes averaged only a very little higher than in the poorly nourished cases.

In making the differential counts no qualitative changes of any moment were noted in any of the cases. Occasionally poikilocytosis, and now and then a single normoblast or a myelocyte, was found.

Paralytic attacks occurred in three cases. No appreciable change was observed in the erythrocytes near these times. In Case IX. the count was made at the time of the first attack, about six hours after the seizure; at the second, eighteen hours before; at the third, twenty hours afterward, and at the fourth, three days later. In Case I. the examination was not made until forty-eight hours after the attack. In Case V. the count was made a few hours after the termination of an epileptiform status of twenty-four hours' duration.

Leukocytes. The study of the leukocytes does not show uniform results. In the cases in which the study extended over many months, the leukocytes presented a gradual fall in three cases, in three cases they were low at the time of the first examination and continued low, while in three cases they varied throughout the entire period. But in all of these nine cases just preceding, coincident with or following the onset of the terminal state, there appears a rise in the number of the leukocytes, which in all but two reaches a leukocytosis. This leukocytosis varies from 10,700 to 27,000. In the two cases which did not reach a leukocytosis there is a rise in one of 1000 and in the other of 3000. In three cases the height of this leukocytosis occurs before the final examination; in Case IX. there is a fall of 3000 in the last four days; Case V., a fall of almost 3000 in the last four days; and in Case I., a fall of 10,400 in the last five days. In the two cases in which the examinations are confined to the terminal state, there is in one a gradual rise from 6300 to 25,000, and in the other a leukocytosis which rose from 10,000 to 14,000.

The paretic states of excitement, of stupor and quiescence, exclusive of the terminal states, did not present any characteristic change. In the four periods of stupor—two cases— there was a constant leukocytosis in one, an average normal count in two, and a low normal in one, but in two of these periods a leukocytosis appeared transitorily. In six periods of excitement—five cases—there was an average hypoleukocy-

tosis in three, an average normal count in two, and a leukocytosis in one. Besides this a leukocytosis appeared transitorily in one period of excitement. In the nine periods of quiescence—eight cases—an average normal count was present in four, a leukocytosis in one, a hypoleukocytosis in two, low normal in one, and a high normal in one, but in seven of these periods a moderate leukocytosis appeared temporarily.

The percentage of the different forms of leukocytes, shown by the differential counts, presents a striking abnormality. A uniform pathological increase of the polymorphonuclear variety occurred in ten of the eleven cases. In this one, Case VIII., the percentage of polymorphonuclear leukocytes remained within normal limits with two exceptions; once it fell to 53.8 per cent., and once it rose to 71.8 per cent. This pathological increase became more pronounced and reached its climax, with one exception, during the terminal stage. In Case II. the highest point is touched during a stage of excitement some months previous to the terminal state, but the average highest percentage occurred during the terminal state.

Plasma cells were carefully looked for in the differential counts, but never encountered. This observation is of importance because of the prominent rôle played by these cells in the vascular changes in the brain, which has come to be regarded as a pathognomonic condition.

The opportunity for observing the condition of the leukocytes near paralytic attacks was limited, as in the eleven cases only six attacks occurred—four in Case IX. and one each in Cases I. and V. In Case I., in which the count, made two days after the attack, was 8300, it is practically of no value. In Case V. the count, made a few hours after the termination of an epileptiform status of twenty-four hours' duration, was 17,200. This was in the terminal state, and five days later, three days before death, the count had dropped 3000. In Case IX. a count was made six hours after the first attack and showed a leukocytosis of 14,000. One week later the count was 19,000 without any apparent reason, except that the patient was still in stupor. The count was made in the second attack twenty-four hours later and showed a leukocytosis of 13,900, which was a rise of over 7000 above the average of the preceding weeks. Two days later the count was 14,600. In the third attack the count made eighteen hours before was 10,300, while for the two previous examinations it was under 7000, and the two subsequent examinations under 8500. In the count made three days following the fourth attack, which was during the terminal state, the leukocytosis reached only 10,000, which was a rise of 2000 over the previous count.

In reviewing the blood changes observed in the hæmoglobin and erythrocytes, there are only two conditions requiring special comment: the progressive moderate anæmia, and the tendency to a polycythæmia and an increase in the percentage of the hæmoglobin in the terminal

state. The anæmia, which is more apparent in the hæmoglobin than in the red cells, is similar to that which accompanies chronic diseases; as, chronic nephritis, cirrhosis of the liver, and syphilis, except that it is less pronounced. It is in accord with the progressive atrophy of the nervous system accompanied by a gradual and complete loss of function, as well as atrophy and arteriosclerotic changes occurring in the internal organs. The tendency for this anæmia to disappear and to be replaced in the terminal state by a progressive increase in both elements, which in some cases passed the normal limits, does not, as far as recorded,[1] find its counterpart in other diseases, and is more difficult of explanation. The most rational explanation would be that it was due to a concentration of the blood, dependent upon a lack of ingestion of fluids and food during the terminal period. This did occur in the paretics during the latter part of the terminal period, and in some cases the abstinence was complete during the last few days.

In order to determine the importance of this factor several moribund cases suffering from inanition were studied. In six such cases in which the examination was made from four to twenty-seven hours ante-mortem, and in which there was an absence of the ingestion of food and water, as well as an absence of temperature or demonstrable inflammatory condition, the hæmoglobin was found to be low in all cases except one (93 per cent.). The erythrocytes in these cases were within normal limits except in this one case, in which they reached 6,155,000. Sluggish circulation was evident in the moribund cases as well as in the moribund paretics, by the slow flow of the blood and by the appearance of an extremely dark-colored drop at the point of puncture. Judging from these facts one feels safe in the assumption that the high percentage of hæmoglobin and the tendency to a polycythæmia of the terminal paretic state is not due to concentration of the blood dependent upon lack of ingestion of food and fluids or to the weakened heart's action and sluggish circulation. Furthermore, this condition of the paretic blood was in the majority of cases coincident with the onset of the terminal state and was in existence some days or weeks before the moribund state appeared.

The two pathological conditions observed in the leukocytes which merit comment are the appearance of a terminal leukocytosis coincident or nearly so with the terminal mental state and the presence of a leukocytosis accompanying paretic attacks of an epileptiform nature. In considering the terminal leukocytosis one must eliminate the presence of any inflammatory conditions which might give rise to it. In Case IX. bronchopneumonia appeared two days before death. The final count was taken ten hours later and showed a fall in the leukocytes from 13,700 to 10,700. With this exception there was no physical

[1] Prof. Ewing informs me that he has observed a somewhat similar tendency in isolated cases of cancer and of tuberculosis.

sign of any inflammatory process in the five cases not examined post-mortem, and no pathological evidence of it in the six cases in which an autopsy was performed.

This leukocytosis should not be confounded with the moribund leukocytosis mentioned by Cabot and other writers, as it appears some time before the moribund state. In accord with their statements it might be added that our six moribund cases, examined from four to twenty-seven hours ante-mortem, showed a leukocytosis varying from 13,000 to 17,000, being highest in the cases four and five hours ante-mortem. Moribund leukocytosis is believed to arise either from stasis or from terminal "intoxication." The former explanation cannot apply to prolonged terminal paretic leukocytosis, as the sluggish circulation and weakened heart action did not appear until just previous to death. The preponderance of experimental evidence goes to prove that leukocytosis should be regarded as a reaction to the presence of a chemical substance in the blood, the function of the leukocytosis being to remove these substances.

The only chronic non-febrile non-inflammatory disease process comparable with dementia paralytica in which a terminal leukocytosis has been observed is chronic nephritis, terminating in uræmia. In this disease Cabot found an absence of leukocytosis in the great majority of cases during the progress of the disease until the uræmic state when leukocytosis appeared in thirty-four of forty cases. This concurrence is most significant, not only in establishing the toxic origin of the terminal state and its leukocytosis, but also the toxic origin of the disease.

The presence of the leukocytosis accompanying paralytic attacks has already been established by Capps. Our limited observations on this matter simply bring additional evidence. In explanation of this phenomena, here again the only recourse is to the toxic theory. The only disease presenting symptoms comparable with the paralytic attacks of dementia paralytica is idiopathic epilepsy. The blood conditions in this disease have been studied by Kroubmiller and Pugh. Kroubmiller[1] studied twelve cases, and claims that at the time of the attack the total quantity of leukocytes is increased and that the increase diminished with every new attack. It is highest one hour after the attack. This increase is due to the relative and absolute increase in the lymphocytes with a relative decrease of the other cells. Pugh[2] studied twenty cases of idiopathic epilepsy. His observations were confined to a single examination from one to twenty-four hours after the occurrence of one or more convulsions in seventeen of the cases, and in three cases an examination also in the interparoxysmal period. He found that a leukocytosis occurred following seizures, which diminished with each convulsion following the first and was less marked in epileptic status.

[1] Idem cit.

[2] Brain, Winter, 1902.

In this leukocytosis there was an increase in the small and large lymphocytes and a diminution of the polymorphonuclear variety.

These observations in epilepsy, which are in accord with the results of Capps and our own in dementia paralytica, add further weight to the toxic theory of the origin of this disease.

The question naturally arises, if this theory be true, Why are not the states of paretic excitement and stupor, which clinically seem to indicate an intensification of the toxic state, accompanied by a leukocytosis? It is a recognized clinical fact that the paralytic attacks are regularly followed by greater mental impairment. The same is true of the excited and stuporous states, at which times the disease usually makes greater inroads upon the mentality of the patient. Furthermore, a similar condition appears to exist in the terminal state whether the outward manifestations are those of excitement, stupor, or simple inanition. The only explanation for the absence of a leukocytosis in the paretic excitement and paretic stupor not terminal is that the toxic state is not intense enough to produce it.

A further pathological change which occurs in striking uniformity is the increase of the polymorphonuclear variety of leukocytes throughout the course of the disease, for which we can offer no explanation.

The results of this systematic examination of the paretic blood corresponds with those obtained by earlier investigators in reference to the progressive anæmia, but they controvert the observation of Smyth that there is a cessation of the progressive fall of hæmoglobin during periods of great exaltation. The recorded observations on the leukocytes have been: a diminution at the end (Macphail), a diminution in seven of fourteen cases (Jelliffe), a slight increase (Somers), a moderate leukocytosis, except near the onset (Capps), and leukocytosis with the exalted state (Jelliffe). Our study does not accord with any of these views, though examinations made irregularly during the course of the disease in any of our cases might easily have brought results in accord with all of them, except those of Capps in reference to the leukocytosis accompanying paralytic attacks. The observation of Jelliffe that a leukocytosis accompanies exalted conditions is improbable, as it occurred in only one of six exalted periods.

Conclusions. Dementia paralytica is accompanied by a moderate and progressive anæmia, involving, especially, the hæmoglobin and becoming more marked as the disease progresses.

The terminal state of the disease is accompanied by a rise in the hæmoglobin, erythrocytes, and a leukocytosis.

Paralytic attacks are accompanied by a leukocytosis.

Throughout the disease process there is a pathological increase of polymorphonuclear leukocytes which reaches its height during the terminal state.

States of paretic excitement, stupor or quiescence, not terminal, are not accompanied by any characteristic blood changes.

The presence of a leukocytosis accompanying the terminal state and paralytic attacks is significant evidence in favor of the toxic origin of the disease.

I desire to express my appreciation of the faithful work done by Messrs. Burr, Ward, and Stone in making the blood-counts, and particularly the assistance given by Mr. H. C. Stone in compiling the statistics of the counts and in arranging the histories of the cases.

The accompanying tables represent only the terminal stage of the disease, and in some cases a part of the period just preceding.

TABLE I.

Month of disease.	Hemoglobin.	Erythrocytes.	Leukocytes.	Poly. leukocytes.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Weight.	Temperature.	Stages of the disease.
Case No. 1.										
25th mo. 4th	77	4,613,000	5,000	78.6	18.6	2.2	0.6	143	Normal	Moderate excitement.
25th " 11th	70	4,653,000	5,800	81.8	12.6	5.6	0	141	"	
25th " 18th	85	4,933,000	6,000	83.2	14.0	2.4	0.4	134	"	
25th " 25th	78	5,166,000	7,266	89 6	9.8	2.0	0.6	131	"	
26th " 2d	78	5,584,000	8,300	85.8	10.2	4.0	0	119	"	
26th " 9th	70	5,475,000	11,533	81.2	14.2	4 6	0	118	"	
26th " 15th	82	5,631,000	9,100	92.0	5.8	2.0	0.2	100		Terminal great excitement.
26th " 17th	80	5,688,000	23,900	96.0	2.8	1.2	0	...	[1]	
26th " 19th	93	5,457,000	22,900	95.6	3.0	1.4	0	...		
26th " 22d	92	6,386,000	18,500	92.8	6.0	1.2	0	85		

TABLE II.

Case No. 2.										
17th mo. 9th	72	4,568,000	8,400	85.2	12.2	2.2	0.4	102	Normal	Quiescent.
17th " 23d	80	5,786,000	5,600	83 4	11.4	3.6	1.6	97	"	
17th " 30th	89	5,306,000	10,533	80.8	14.2	4.4	0.6	97	"	
18th " 7th	70	5,671,000	8,400	80.0	13 2	6.0	0.8	94	"	
18th " 15th	62	5,453,000	8,200	79.6	14.0	4.2	2.0	94	"	
18th " 22d	83	5,182,000	9,100	77.6	16.8	4.6	1.0	92	"	
18th " 29th	67	4,888,000	8,400	90.0	6.6	3.4	0	88	"	Terminal stupor.
19th " 4th	82	5,982,000	16,100	86.4	9.8	3.2	0.6	79	"	

TABLE III.

Case No. 4.										
18th mo. 2d	65	4,515,000	7,000	78.8	16.0	5.0	0.2		Normal	Terminal stupor.
18th " 16th	68	4,916,000	10,160	81.6	15.2	2.4	0.8	[2]	"	
18th " 31st	70	4,222,000	8,700	86.2	9.4	4.4	0		"	
19th " 12th	70	4,697,000	14,660	94.2	8.8	2.0	0		"	

TABLE IV.

Case No. 5.										
16th mo. 5th	83	5,133,000	7,600	81.2	13.1	4.5	1.1	111	Normal	Excitement.
16th " 12th	83	5,442,000	7,600	82.2	10.4	6.0	1.4	110	"	"
16th " 19th	85	5,622,000	6,700	84.0	10.3	4.0	1.7	110	"	"
16th " 26th	85	5,724,000	11,400	84.8	10.0	4 4	0.8	109	"	"
17th " 2d	86	5,624,000	11,300	84.4	11.6	3.6	0.4	...	"	"
17th " 5th	76	5,162,000	17,200	93.2	3 6	3.2	...	...	"	Terminal stupor.
17th " 9th	86	6,333,000	14,267	93.4	4.0	1.4	1.2	85	"	

[1] Could not be taken.

[2] Could not be taken.

TABLE V.

Month of disease.	Hæmoglobin.	Erythrocytes.	Leukocytes.	Poly. leukocytes.	Small lymphocytes.	Large lymphocytes.	Eosinophiles.	Weight.	Temperature.	Stages of the disease.
Case No. 6.										
7th mo. 31st	85	5,488,901	6,300	82.2	12.8	4.6	0.4	[1]	Normal	Terminal stupor.
8th " 10th	70	4,573,000	6,500	86.2	7.8	5.4	0.6		99.4	
8th " 17th	68	4,769,000	10,000	85.0	9.4	4.4	1.2		98.6	
8th " 26th	60	3,711,000	17,720	93.0	2.6	4.4	0		.....	
9th " 2d	65	4,484,000	25,000	83.0	14.0	2.2	0.8		96.4	

TABLE VI.

Case No. 7.										
19th mo 18th	70	4,516,000	6,600	70.6	21.2	6.2	2.0	113	Not taken	Excitement.
20th " 6th	85	5,293,000	5,533	66.0	24.4	6.8	2.8	107		"
20th " 20th	86	5,053,000	5,030	71.8	24.6	2.4	1.4	100		"
21st " 8th	76	4,244,000	6,300	53.8	37.2	8.2	0.8	111		"
21st " 22d	78	4,400,000	5,900	54.4	39.0	3.6	3.6	112		"
22d " 5th	105	5,089,000	9,060	71.8	20.2	4.2	0.8	104		Terminal stupor.

TABLE VII.

Case No. 8.										
11th mo. 29th	85	5,800,000	7,400	80.4	13.2	5.2	1.2	157	Normal	Quiescent.
12th " 5th	85	4,942,000	10,660	84.0	10.2	4.0	1.8	157	"	
12th " 12th	90	5,408,000	10,900	81.4	13.2	4.0	1.4	155	"	
12th " 19th	97	4,693,000	16,500	92.0	5.6	2.0	0.2	...	"	Terminal excitement.
12th " 26th	102	6,302,000	17,800	79.2	14.6	5.2	1.0	128	"	
12th " 27th	105	6,373,000	17,920	81.8	15.6	1.6	1.0	...	"	
13th " 2d	120	7,551,000	27,000	91.6	6.0	2.0	0	121	"	

TABLE VIII.

Case No. 9.										
29th mo. 29th	82	5,547,000	7,750	76.6	17.2	4.2	2.0	145	.....	Terminal stupor.
30th " 5th	73	4,500,000	8,666	76.4	15.4	6.0	2.2	145	97.2	
30th " 12th	80	4,700,000	10,000	87.4	7.0	5.2	0.4	139	99.6	
30th " 18th	78	4,131,000	18,730	84·8	11.6	3.2	0.4	129	99.6	
30th " 22d	...	3,600,000	10,700	...	...	...	...	...	105.0	

TABLE IX.

Case No. 10.										
24th mo. 8th	65	4,538,000	5,100	76.4	20.4	2.6	0.6	161	Normal	Terminal stupor.
24th " 15th	78	4,889,000	7,000	65.0	28.2	5.6	0.6	...	"	
24th " 22d	80	5,333,000	8,200	80.4	12.8	5.2	1.6	...	"	
24th " 30th	90	6,271,000	15,860	86.2	6.8	6.8	0.2	107	"	

TABLE X.

Case No. 11.										
26th mo. 8th	80	5,533,000	7,860	74.2	22.4	3.2	0.2	144	Normal	Quiescent.
26th " 24th	68	4,862,000	6,000	76.0	19.6	4.2	0.2	137	"	"
27th " 5th	75	4,747,000	8,860	82.2	14.2	3.2	0.4	137	"	"
27th " 19th	80	5,328,800	7,260	81.4	14.8	3.6	0.2	134	"	"
28th " 2d	78	5,333,000	8,800	77.8	17.2	4.4	0.6	130	"	Stupor.

[1] Could not be taken.

REVIEWS.

A Manual of Practical Hygiene. By Charles Harrington, M.D. Second edition. Pp. 760. Illustrated with engravings and colored plates. Philadelphia and New York: Lea Brothers & Co., 1903.

It would be difficult to imagine a book better fulfilling the needs of the general reader and at the same time containing the essentials of a book of general reference on hygiene. The author has considered not only the more generally known phases of the question, but also the recent problems of prophylaxis. The first quarter of this most readable volume is devoted to Foods, with special reference to their nutritive value, and then their contaminations and adulterations, with the more simple methods of detecting the latter. A chapter on the Air follows, giving in detail its normal constituents, extraneous concomitants, and methods of analysis. Then come chapters on Soil and Water, the latter being especially valuable for the clear description of the general principles of water supply and the danger of spread of infectious diseases when this most important subject of public health is carelessly dealt with. Habitations are treated in reference to ventilation, lighting, and plumbing. In logical sequence are discussed the subject of Sewage and Disposal of Garbage; Military and Naval Hygiene and Quarantine are given in their essentials. Of particular interest is the chapter on the Relation of Insects to Human Diseases, in which malaria, yellow fever, and filariasis are detailed in their recent developments. The prevention of disease by means of specific vaccination is dealt with in a thoroughly modern fashion. References to the periodical literature are given in footnotes sufficiently to aid further reading without alarming one by their number. The presentation of the text is excellent, and the book is fully illustrated. In short, it is a volume to which one may go for specific information, and the subjects are presented so attractively withal that he would be apt to turn over the next leaf. F. G. P.

Text-book of Medical Jurisprudence and Toxicology. By John J. Reese. Sixth edition. Revised by Henry Leffmann, M.D. Philadelphia: P. Blakiston's Son & Co.

This useful compendium of toxicology and medical jurisprudence, which has reached its sixth edition, has been brought up to date through the able editorship of its reviser. In his preface to this edition the latter says that "the introduction of numerous synthetic organic bodies, and the extensive use of some of them as household remedies, has given rise to

many instances of accidental and suicidal poisoning. Current medical literature shows that phenol is becomiug one of the most common agents of self-destruction, while the extensive use of water-gas greatly increases the list of accidental poisonings." The difficulties and perplexities of the analyst are greatly increased by the absence of tests which are conclusive of the presence of many of these synthetic bodies, and those of the post-mortem examiner rendered only less pronounced through the want of distinctive appearances upon which their action is unmistakably to be based.

In the chapter on the Examination of Blood Stains a brief reference to the use of the precipitin test is made. This test has come, within the relatively short period since its introduction into medicolegal use, of such great importance that a fuller treatment in the volume before us would have seemed advisable. In view of the frequency with which blood stains come up for consideration by the medicolegalist, and the high importance of an indubitable statement as to their nature, minute directions for carrying out the test, its scientific and practical limitations, and perhaps a brief reference to cases in which it has already been employed, might not have been out of place.

In the section on Burns and Scalds the cause of death in severe cases is still given as the extensive loss of the skin surface and interference with the function of secretion and heat regulation. This view is not upheld by more recent studies in which more definite effects are easily ascertained and are sufficient to account for the severe and fatal results. The production of extensive thrombi and their consequences as well as the action of "tissue poisons," the outcome of tissue destruction, are entirely competent to explain the otherwise mysterious symptoms following upon severe superficial burns.

The volume before us has many valuable features that far outweigh the very occasional omissions of more recent knowledge on a few of the subjects included in its scope. It can be recommended in its new edition as heartily as ever in its older editions.

BIOGRAPHIC CLINICS. The Origin of the Ill-health of De Quincey, Carlyle, Darwin, Huxley, and Browning. By GEORGE M. GOULD, M.D. Philadelphia: P. Blakiston's Son & Co., 1903.

IN this unique little work Dr. Gould not only studies the lessons to be drawn from the lives of the five men whose names appear upon his title-page, but also deducts from the study of their lives the practical points which bear upon the life-histories of all our patients. In each of the instances which Dr. Gould has chosen for his study there is very complete biographical material at hand, from which it is possible to construct an intimate personal history of the various pathological conditions presented. In each instance the cause of the profound gloom which at times enwrapped them, and of their constant complaint of dyspepsia, vertigo, and innumerable other physical ills, the author thinks are distinctly traceable to the eye, stating the reason as uncorrected astigmatism. This theorem he supports by many ingenious arguments.

The only real criticism to our mind which can be offered in contradiction to what Dr. Gould so ably advances is that at times his enthusiasm

has led him to make inferences which we would regard as not wholly supported by the facts at hand; thus in pointing out that the long walks, rides, etc., which always benefited each one of the victims whose case is described in this book did them good by the rest of the eyes which was necessarily induced, we are inclined to think that possibly also the long walks, rides, etc., might be held to have benefited the liver and general condition quite as much as the eyes.

There are a few curious typographical errors. On page 160 Norris and Oliver's *System of Diseases of the Eye* is attributed to Morris and Oliver. On page 184 Dr. Pray is said to have described his test type for the diagnosis of astigmatism in 1869, the bibliographical footnote stating that the paper appeared in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES for January, 1867. The book is one of value to all who do literary work, as well as to physicians, and we sincerely trust that it will meet with the favorable reception it most certainly deserves.

F. R. P.

MANUAL OF GYNECOLOGY. By HENRY T. BYFORD, M.D., Professor of Gynecology and Clinical Gynecology in the College of Physicians and Surgeons of Chicago. Third revised edition, containing 363 illustrations, many of which are original. Pages 598. Philadelphia: P. Blakiston's Son & Co., 1902.

IN this edition the author has brought the subject up to date by the addition of much new matter. The field of gynecology is fully reviewed in a manner which will be found quite satisfactory to the medical student and to the busy practitioner who may wish to refresh his memory. The system of marginal notes and the avoidance of repetition by the use of so many text references may be of value to the student who is preparing for an examination, but it is not good literary form, and makes awkward and disjointed reading. The book is extensively and well illustrated; the illustrations of many pathological conditions being selected from the best works on the subject are especially valuable. The teaching is wise and conservative, and while there are many views expressed which are still open to discussion, especially under the head of pathology, still there is little to criticise, and the book is a safe guide for the student and the practising physician, for whom it is intended.

J. B. S.

A MANUAL OF OBSTETRICS FOR STUDENTS AND PRACTITIONERS. By W. P. MANTON, M.D., Adjunct Professor of Obstetrics and Professor of Clinical Gynecology, Detroit College of Medicine. Philadelphia and New York: Lea Brothers & Co., 1903.

As an aid to the student or practitioner of medicine, Dr. Manton's book will prove of much value. It is, as its name implies, an epitome or condensation of the essentials of the science of obstetrics, and the author has so compiled his volume as to render it much more complete than it is usual to find such works. A feature which will be found of

much service to students preparing for examinations is a set of questions at the end of each chapter, on its contents. The entire work reflects much credit upon its author, and, although intended, primarily, for the use of students, it will be found a most handy little work of reference for the practising physician, containing as it does the most advanced work in the science and art of obstetrics. W. R. N.

BURDETT'S HOSPITALS AND CHARITIES, 1903. Being the Year Book of Philanthropy and the Hospital Annual. Containing a review of the Position and Requirements, and chapters on the Management, Revenue, and Cost of the Charities. An exhaustive record of Hospital work for the year. It will also be found to be the most useful and reliable guide to British, American, and Colonial Hospitals and Asylums, Medical Schools and Colleges, Nursing and Convalescent Institutions, Consumption Sanatoria, Religious and Benevolent Institutions, and Dispensaries. By SIR HENRY BURDETT, K.C.B. London: The Scientific Press (Limited). New York: Charles Scribner's Sons.

THIS monumental work has an indispensable value not only to physicians, but to everyone interested in charitable or philanthropic enterprise. It is so well known that a detailed description of the plan on which it is written is unnecessary; suffice it to say that its pages constitute a complete directory to medical and charitable institutions throughout the world. No efforts are spared to make the information contained within it accurate, and it is thoroughly reliable in every respect. It is hard to estimate the debt of gratitude due to Sir Henry Burdett and his associates, not only from the medical profession, but from the entire world.

In the preface mention is made of the fact that a well-known philanthropist had written to the editors stating how much this work had aided him in the distribution of enormous sums of money among the hospitals of London. This is an indication of the beneficent operations of such a publication. To lawyers and others concerned in the drawing up of wills, bequeathing sums to charities, this work furnishes a reliable guide. Let us sincerely hope that the good work which it has done in the past will be continued in the future. F. R. P.

THE REFRACTION AND MOTILITY OF THE EYE. FOR STUDENTS AND PRACTITIONERS. By WILLIAM NORWOOD SUTER, M.D., Assistant Surgeon, Episcopal Eye, Ear, and Throat Hospital, Washington, D. C. Illustrated with 101 engravings in the text and 4 plates in colors and monochrome. Philadelphia and New York: Lea Brothers & Co., 1903.

ALL works of this kind must give a certain body of truths. These present little scope for originality. Successful treatment expresses the facts and the reasons upon which they are based in a way comprehensible to the reader, for which the work is intended—in this case students and practitioners of medicine. The most concise and accurate method

of dealing with the optics of refraction is, of course, by mathematics; as this must be largely eschewed, the problem is this: to express mathematical ideas and methods in ordinary language, clear enough for the non-mathematical reader to comprehend. This is never easy, requiring technical knowledge and the teacher's power of exposition in a marked degree, and even then not always possible. We ask, then, when we meet a work of this kind, With what success has the writer solved the problem? In Dr. Suter's book a very high measure of success has been attained. The subject has been so presented that without the sacrifice of accuracy, but a minimum of mathematical knowledge is required of the reader.

In expounding the fundamentals the references are frequently made directly to the works of original experimenters. Interesting historical notices abound. Rule of thumb work is conspicuously absent.

Part I. gives the theory of refraction, eight chapters, somewhat less than a third of the entire work. It is less mathematical than the introductory chapter of Landolt, making no references to the formal language of trigonometry.

Part II., two chapters, deals with refraction and motility of the normal eye. Tscherning's theory of the accommodation is given, but not indorsed.

Parts III. and IV. deal with errors of refraction and disorders of motility. The directions for prescribing correcting lenses in the various forms of ametropia are clear and judicious.

The operative treatment of myopia is very properly stated to be limited in its application.

Heterophoria is fairly described, tests, symptoms, etc. We are glad to note that the absurd claims which have been made for this condition find no indorsement whatever.

The language of the book is clear and the style direct. T. B. S.

INTERNATIONAL CLINICS. Edited by A. O. J. KELLY, A.M., M.D., Philadelphia, Pa., U. S. A. Vol. I. Thirteenth Series, 1903. Pp. 306. Philadelphia: J. B. Lippincott Co.

IN this volume diseases of the circulatory system are well represented by articles by Osler on "Aneurism of the Descending Aorta"—a careful study and more valuable from the collated cases presented in abstract; Wilcox, on "The Treatment of Cardiac and Vascular Fibrosis, Hodgson's Disease, the Treatment of Anæmia, Anæmic and Vascular Murmurs"; Satterthwaite, on "Nauheim Methods in Chronic Heart Disease, with American Adaptations"—a thoroughly practical and scholarly paper, reflecting a large experience. The remaining papers in treatment are those by Finger, who offers the treatment on "Chronic Urethritis," and Fussell, on the "Treatment of Diphtheria," who sees in his title more than the antitoxin question, and gives good advice as to accessory treatment and complications. Medicine is well represented by Billings, with a thoughtful paper on "Primary Intestinal Tuberculosis"; Einhorn takes up "Pyloric Obstruction, Gastric Dilatation, and Gastric Stagnation"; Keen and Senn present a wealth of well-digested surgical information of various topics, among which the

nervous system plays a prominent part—tic douloureux, traumatic epilepsy, concussion of the brain, and hydrocephalus. Tonnesco, on "The Enduring Results of Total Bilateral Resection of the Cervical Sympathetic in Basedow's Disease," gives his conclusions as follows: "Total bilateral resection of the cervical sympathetic is the most effective means for the relief of primary Basedow's disease. It is, besides, the only rational operation if we concede that this disease is due to functional rather than to organic changes in the system. Cervical sympathectomy is the only operation that relieves the main symptoms of the disease, and at the same time lessens or removes the accessory conditions that have developed during the affection. The effects produced by this operation are such as to bring about complete and lasting relief." Thus, we have the last word from the surgical side of the question, and the medical is quite ready to accept any method which offers hope for a more enduring relief, or indeed cure. Ross, on "Acquired Umbilical Hernia in the Adult," and Manley, on "The Greater Importance of the Organs in Right as compared with those of the Left Lateral Half of the Abdomen," complete the section devoted to surgery. Pediatrics in a single article, Thomson, on "The Causation, Treatment, and Prognosis of Convulsions in Young Children," and Orthopedics, likewise a single, very readable paper, by Shands, on "The Treatment of Weak Feet and Flat Feet," bring the reader to two unusual contributions; that is, King, on "Functional Reversion and its Import in Medical ractice," and Ballantyne, on "The General Principles of Embryology." The remainder of the volume is occupied by a review of the progress of medicine during the year 1902 by Watson and Cattell, in which various topics in medicine, therapeutics, and surgery are taken up. As compared with reviews of progress to be found in the best of the journals or year books this is, of course, limited and incomplete, but as representing that which the reviewers regard as first among the foremost we accept it, and congratulate them upon an excellent fulfilment of their task. We have noted the papers in this volume in more than usual detail, because they present a remarkable degree of excellence and interest. With this volume we recognize the accession of a new editor, who, if he shall maintain the high standard which he has set, will more than meet the expectations of the numerous and critical readers of *International Clinics*. R. W. W.

THE SURGICAL TREATMENT OF GASTRIC AND DUODENAL ULCERS. By B. G. A. MOYNIHAN, M.S. Lond., F.R.C.S. Eng.; Senior Assistant Surgeon, Leeds General Infirmary; Consulting Surgeon to the Skipton Hospital and to the Mirfield Memorial Hospital, etc. Pp. 83, illustrated. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

THE reading matter of this monograph consists of forty pages of text with ten illustrations and diagrams, followed by the histories, in table form, of more than 100 cases submitted to operation. The book is attractive in appearance, printed on good paper in clear type. Mr. Moynihan is to be congratulated on the way he handles his subject, for in clearness, terseness, and brevity his style could not be excelled, and yet,

at the same time, the reader is never in doubt as to the opinions expressed and the author's idea of the subject under discussion.

The subject-matter is divided under four headings: Perforation of Gastric and Duodenal Ulcers, Hemorrhage, Chronic Ulcer, and Hour-glass Stomach. Under these headings the symptoms and treatment are discussed, with special reference to the time for and character of the operation to be performed. He calls attention to the fact that gastric ulcer is seldom single and almost invariably multiple, and for this reason condemns all operations which attempt the extirpation of a given ulcer, reasoning that where many ulcers are present it is impossible to tell which is the offending one. His choice of operation for this reason is almost invariably a gastroenterostomy, and his reasons for preferring this to pyloroplasty are, to the reviewer at least, convincing. Under the subject of Hour-glass Stomach he strongly combats the hypothesis that many of these cases are of congenital origin, believing, and proving this also by his dissections, that such conditions result most frequently from cicatricial contraction of ulcers or from localized inflammatory products outside of the stomach wall. His method of gastroenterostomy is safe, simple, and easy of execution, with the promise of the best after-results. The fact that he has done over eight gastroenterostomies with but one death makes his opinions worthy of the deepest thought, and stamps his method as a thorough and complete one.

This book will be of the greatest value to the abdominal surgeon and also to the practising physician; for to the latter it will be of much assistance in deciding when medical treatment should cease and surgical begin. R. G. L.

DISEASES OF THE PANCREAS AND THEIR SURGICAL TREATMENT. By A. W. MAYO ROBSON, F.R.C.S., Senior Surgeon, Leeds General Infirmary; Emeritus Professor of Surgery, Yorkshire College, Victoria University; Member of Council and Hunterian Professor, Royal College of Surgeons of England; and B. G. A. MOYNIHAN, M.S. (London), F.R.C.S., Assistant Surgeon, Leeds General Infirmary; Consulting Surgeon to the Skipton Hospital and to the Mirfield Memorial Hospital; Arris and Gale Lecturer and Member of the Board of Examiners in Anatomy for the Fellowship, Royal College of Surgeons of England. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

UNTIL recently little could have been written upon the diagnosis and treatment of pancreatic diseases, but during the past five years, and particularly since the publication of Fitz's paper on "Pancreatitis," in 1899, this subject has received a vast amount of attention both from surgeons and medical men. To the authors of the volume under consideration, and particularly to Robson, is due to a considerable extent the progress made in the surgical treatment of the various pathological conditions of the pancreas. Of course, there is still much to be learned about these conditions, as well as about their treatment, and the aim of the authors has been not to say the last word regarding the pancreas, but rather to present the present status of the subject in as clear a light as possible to the medical profession. It is pleasing to note that they have dedicated this volume "To the Surgeons of America in Cordial Recognition of Their Work."

The first chapter contains the descriptive and surgical anatomy of the pancreas, and the second deals with the experimental work which has been done on the pancreas, particularly regarding the relation of diabetes to diseases of the pancreas. The chapter on Injuries of the Pancreas is interesting, a number of cases having been gathered from the literature illustrating lacerations and other injuries. In none of the recorded cases was it possible to make a diagnosis of laceration of the pancreas before operation or death. Injury of the organ is seldom unaccompanied by extensive injury to other abdominal viscera, and consequently treatment of the condition is rarely possible. As a result of laceration of the pancreas, however, certain sequelæ may occur, such as absence of the pancreas or distention of the lesser peritoneal cavity due to the pouring out of blood and possibly pancreatic secretion. The author states that there have been eight well-investigated cases of prolapse of the pancreas.

Four chapters are devoted to the various forms of pancreatitis, and it is this condition which appeals most to both physician and surgeon. Pancreatitis is divided into acute, subacute, and chronic. The authors show that the pancreatic ducts participate in the same inflammatory processes as do the bile-ducts. They state that "the most satisfactory evidence at present of deficient pancreatic juice in the bowel is afforded by the abundance of undigested muscle fibre in the motions of a patient not suffering from diarrhœa after a meat diet; and by the absence of carbolic acid and salicin in the urine when 60 grains of salol are taken in divided doses during the day." The study of pancreatitis under the clinical heads of acute, subacute, and chronic, does not interfere with Fitz's pathological classification of acute pancreatitis into hemorrhagic, suppurative, and gangrenous. Both the symptoms and pathology of the various forms of pancreatitis are well illustrated by the reports of a number of interesting cases.

The closing chapters deal with pancreatic calculi, cysts, and new-growths.

This work has been well prepared by thoroughly competent authorities, and undoubtedly presents the subject in a most useful manner to both surgeons and physicians. J. H. G.

DISEASES OF THE SKIN. A MANUAL FOR STUDENTS AND PRACTITIONERS. By JOSEPH GRINDON, Ph.B., M.D., Professor of Clinical Dermatology and Syphilis, Washington University; Dermatologist to the O'Fallon Dispensary, St. Louis Mullanphy Hospital, St. Luke's Hospital, etc. Philadelphia and New York: Lea Brothers & Co., 1902.

THIS manual of nearly 400 pages—one of a series of "pocket text-books"—stands midway between the quiz compend and the more formal and elaborate treatises. It aims to present the essentials of Dermatology in a concise manner, and is intended, as we learn from the preface, not only for the student, but for the practitioner of medicine. The symptomatology, pathology, and treatment of the various diseases of the skin are discussed in a clear and, for the most part, satisfactory manner, although, necessarily, with brevity.

The author regards pityriasis rubra and dermatitis exfoliativa as simply varieties of the same affection. We do not believe, however, that the grave and often fatal malady described by Hebra under the former title is the same as the exfoliative inflammation of the skin which not infrequently appears as the sequel of other inflammatory diseases, such as psoriasis, and pursues a uniformly benign course.

Eczema is looked upon as a symptom-complex rather than a distinct disease, a manner of view which seems to find favor with recent writers. In considering the predisposing causes of this Protean disease the author is inclined to accept the existence of the so-called dartrous diathesis of the older French writers. Since no one, not even the French themselves, has ever been able to explain, satisfactorily, what is meant exactly by dartre, it hardly seems worth while to resurrect this ancient notion. Renal incompetence is stated to be an important factor in the causation of eczema in those past middle life. It would seem as if this ought to be true, but, as a matter of fact, no one has yet been able to demonstrate any definite relation between insufficient urinary excretion and eczema. Even in such an affection as chronic interstitial nephritis, in which renal incompetence may reach an extreme degree, eczema is decidedly the exception rather than the rule.

In the treatment of erythematous lupus the author urges that care be taken that the remedies used shall do no harm, even if they do no good—a much-needed caution, since the inexperienced are apt to make bad worse by injudicious and too active treatment. We do not find any mention made of large doses of quinine internally in the treatment of this very obstinate affection—a remedy which recent observation has shown to be of decided benefit in many cases.

Although necessarily lacking in detail because of its size, the manual will be found a useful one by both student and practitioner. M. B. H.

THE ROENTGEN RAYS IN THERAPEUTICS AND DIAGNOSIS. By W. A. PUSEY, A.M., M.D., of Chicago, and E. W. CALDWELL, B.S., of New York. Philadelphia, New York, and London: W. B. Saunders & Co., 1903.

IN this work the authors have presented clearly and simply their opinions derived from comparative study and their personal clinical and laboratory experience. Sufficient has been taken from the literature of the subject to afford the reader a comprehensive view of the influences which have led them to form the personal opinions expressed, the citation of the journals and authorities permitting the reader to follow such other opinions as he fancies further. Without any desire to be dogmatic they present a comprehensive work, based upon their personal experience, that will enable the reader to acquire by clinical study the knowledge which is essential to the proper employment of this method of diagnosis.

Part I. X-ray Apparatus and its Uses in Diagnosis. Without entering too much into electrical detail, the authors have given the results of their personal experience as trained electricians in adapting apparatus to the diagnostic needs of the surgeon. As is to be expected this por-

tion of the work is richer in electrical technique and methods than in the surgical interpretation of the results that are obtained. It deals with the question of apparatus, etc., with an appreciation of the needs of the surgeon, and is, therefore, of great value, since things electrical are explained clearly in language the surgeon can understand.

Part II. The Therapeutic Application of X-rays. After a comprehensive résumé of the literature of the subject the authors give valuable illustrations of its application culled from their personal experience. The chapter on the Effects of X-rays on Tissue is particularly valuable in teaching the novice what to expect as therapeutic manifestations when commencing treatment. In describing their technique they have fully realized the impossibility of dealing with any other technique than their own, and make the reader realize that their deductions apply only to their own method, and that clinical experience is the only foundation as yet upon which each worker must build his own method in therapeutics. This element of personal clinical experience cannot be dwelt upon too strongly. No matter how explicit and valuable the work or the instruction the novice has received, he should fully realize that he is always dealing with a powerful agent that is capable of doing harm as well as good, and must often be used with its utmost power to attain the desired results. A study of this work will show why the expert with this method can obtain results that are impossible to the novice, and will lead to the careful instruction of those asked to take up this work by hospitals before they are placed in charge.

The work will be an inspiration to the student to the scientific study of the X-rays, as well as a ready guide and book of reference.

C. L. L.

TUBERCULOSIS. Recast from Lectures delivered at Rush Medical College, in Affiliation with the University of Chicago. By NORMAN BRIDGE, A.M., M.D. Philadelphia, New York, and London: W. B. Saunders & Co.

IT is not an easy task to write interestingly on a well-worn topic like tuberculosis, yet it is in these very subjects that an original contribution is particularly welcome. While there have been no material additions to our knowledge of pulmonary tuberculosis within recent years, the interest in the disease on the part of the public as well as the profession has never been keener than at the present time, since the vital importance of effective precautionary measures and of rational methods of treatment has come to be appreciated even by our municipal authorities. It is needless to dwell on the author's presentation of the pathology, bacteriology, and other formal parts of the work except in general approbation of his treatment of these subjects. The chief interest of the book lies in the personal element and spontaneity that is or should be the characteristic of clinical teaching: a general acquaintance with the fundamentals of tuberculous lore—the author has defined the meanings of these much misused terms, *tuberculous* and *tubercular*—on the part of his readers or, rather, his hearers.

He distinguishes no less than eight clinical forms of pulmonary tuberculosis, and it must be confessed that some of these distinctions

are rather finely drawn, although always instructive, and there is, unfortunately, no hint of the relative frequency of each. With four of these the student will be familiar from his text-book reading, the fibrous form, or "fibroid phthisis"; the circumscribed form, with a distinctly localized lesion, walled off by a fibrous wall, without general spread; the form characterized by cavities, pus absorption, and an overpowering mixed infection terminating in death before there has been time for extension to other organs—so-called "galloping consumption"; and general visceral tuberculosis secondary to a pulmonary atrium. The last member of the group, to which the author would concede the name of "miliary tuberculosis," is described as a pure tuberculous infection, either primary or secondary to a "long-existing quiescent tuberculosis in a circumscribed lung area," distinctly chronic in character, with almost no pus formation, and "only a little fever, which may occur irregularly," and uncertain physical signs. It will be seen that the author's teaching in this respect differs radically from accepted dogmas; indeed, he specifically attacks the conception of miliary tuberculosis as given in text-books, denies the occurrence of high fever in tuberculosis except as a terminal complication, and regards this form as a chronic condition with a stormy ending. The remaining three varieties are described as tuberculosis probably confined to the bronchial mucous membrane, with the most favorable prognosis of all; a "fibrous and dissolving" form with atrophy of septa from pressure on the capillaries, coalescence of contiguous alveoli, and consequent reduction of respiratory space, characterized by resonance instead of dulness and other paradoxical physical signs—a steadily progressive form going on to an inevitable lethal termination; and a form which must surely be rare and in which the infection begins in the right apex, and after complete regression attacks the upper portion of the left lung, with or without recrudescence of the morbid process at the original site, depending on the duration of life.

The chapters on diagnosis contain a number of practical points and warnings against possible errors in observation and interpretation, which are evidently the outcome of the author's personal experience.

Nearly one-half of the little volume is devoted to prophylaxis and treatment, and while, of course, climatic and hygienic methods come in for their full share of attention, the author shows that much can be done in a palliative as well as in a curative way without expatriating the patient. Directions as to personal hygiene and diet are dwelt with at length. In the matter of serumtherapy the author, like most other authorities, is extremely skeptical. R. M. G.

THE INTERNATIONAL MEDICAL ANNUAL. A Year Book of Treatment and Practitioner's Index. New York: E. B. Treat & Co., 1903.

THIS most excellent compendium of the year's work in the medical profession is worthy of high commendation. It is difficult for the compilers of such a book to introduce any very original features, but the editors of the volume under consideration have shown much discretion in the arrangement of their work and in the material which they have abstracted in it. A particularly attractive feature of the volume is the

excellence and large number of the illustrations, many of them in colors. For the practitioner who wishes a handy book in which to look up recent points in medicine we can recommend this as a most useful guide.

J. H. G.

THE DISEASES OF WARM COUNTRIES: A HANDBOOK FOR MEDICAL MEN. By B. SCHEUBE, State Physician and Sanitary Adviser, Greiz; late Professor at the Medical School in Kyoto (Japan). Translated from the German by PAULINE FALCKE, with addenda on Yellow Fever by JAMES CANTLIE, M.B., F.R.C.S., and on Malaria by C. W. DANIELS, M.B., M.R.C.S. Edited by JAMES CANTLIE, Lecturer at the London School of Tropical Medicine, etc. Second revised edition. Philadelphia: P. Blakiston's Son & Co., 1903.

IT is a matter of congratulation that the well-known and authoritative work of Professor Scheube on tropical diseases has been translated into English. The growing importance of a knowledge of tropical disease to American physicians makes the volume peculiarly welcome. The benefit to English medical literature is, moreover, enhanced by the consideration that to a sufficient and discriminating presentation of the knowledge of tropical diseases is added a wide experience in the treatment of many of the diseases dealt with in Professor Scheube's volume. The scope of the volume may be gathered from the several sections into which the matter is divided. The first section deals with the general infections, among which beriberi and dengue, diseases of unknown etiology, are placed alongside of plague and leprosy. What will impress the physician whose experience has been limited to temperate climates, where disease has perhaps been more carefully studied and differentiated, is the use of such terms as "Indian Nasha fever" and "Japanese River or flood fever" to designate disease entities. The first, described by Fernandez, abounds in malarial districts, but is doubtfully due to the *Plasmodium malariæ;* it is, moreover, of very doubtful specificity. The second, described by Balz, and regarded by him as specific in nature, is of unknown etiology, although the "virus" is supposed to cling to the submerged soil of the river valleys. The constancy of a skin eruption appearing on the sixth or seventh day brings it among the exanthemata. The mortality is given variously from 15 to 70 per cent. The second section treats of the diseases due to intoxicants, among which are pellagra, lacquer poisoning, venom poisonings, etc. It may be worth while to allude to lacquer poisoning on account of the resemblance to rhus poisoning. Only the fresh lacquer produces the general symptoms and skin lesions, which consist of slight fever and itching of the skin of the head, face, and limbs, to be followed by œdema and a papular eruption. This resemblance of symptoms to those of *Rhus toxicodendron* poisoning is emphasized by the fact that the lacquer-tree belongs to the same botanical family, its species being *Rhus verniciferæ*. The third section deals with animal parasites, a most important chapter of tropical disease, the fourth of the organic diseases, among which sprue, dysentery, and sleeping sickness are included. There seems little justification for the inclusion of dysentery in this section and its treatment as a disease of wholly unknown etiology. It would have been far better to have sub-

stituted some more distinctive title for that of "organic" diseases, and in view of the fact that the diseases of the group are doubtless infectious in origin, "special infections" might have been a suitable one. It is to be regretted that no reference in the article on dysentery is made to the studies of Shiga and his followers that have added so greatly to our knowledge of the cause of dysentery.

Section five treats of the cutaneous and local diseases, among which Madura foot, tinea imbricata, and pinta (*mal del pinto*), a dermatomycosis, distinguished by spots of different colors, which give to the victims a piebald appearance without causing any disturbance of the general health.

The last section is devoted to a consideration of the cosmopolitan diseases of the tropics, by which is meant the diseases which are common in temperate climates as well.

This work, in itself so important, is increased in value by the addition of a brief chapter on "Malaria," by Dr. Daniels, and on "Yellow Fever," by Dr. Cantlie, and by the many new plates introduced into the translation. F.

DIE ROENTGENSTRAHLEN IM DIENSTE DER CHIRURGIE. By DR. CARL BECK, of New York. Published by Seitz & Schauer, Munchen.

THE work consists of two volumes written in the German language.

Volume I. contains 138 pages, and is devoted to the uses for which the Roentgen rays may be applied in medicine and surgery. The author lays stress upon the value of this method of diagnosis, and takes up systematically the different parts of the body, mentioning the pathological conditions that may occur in each part. He gives very briefly an idea of the technique used in the examination of each part of the body, and in a number of instances illustrates with brief reports of cases.

Volume II. consists of sixty plates, which, with a few exceptions, seem to be inferior.

As a whole, the work presents little that is new, unless it be in the use of the Roentgen ray in the diagnosis of billiary calculi. It is not a work for a beginner, but may be added with profit to a skiagrapher's library. G. E. P.

THE ROENTGEN RAYS IN MEDICINE AND SURGERY. By FRANCIS H. WILLIAMS, M.D., of Boston. Third edition. New York: The Macmillan Company, 1903.

IN this new and enlarged edition Dr. Williams has added much of value both by the increased data derived from his personal experience and by a well-indexed résumé of the current literature of the subject. This feature of the work is particularly valuable, as the student is enabled to turn to the original writing of the authority quoted, in any line of work in which he is particularly interested. C. L. L.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Operative Treatment of Ulcerative Colitis.—Boas (*Deutsche med. Wochenschrift*, 1903, xxix., 196) reports an interesting case of ulcerative colitis cured by operative interference and irrigation of the colon. The patient, aged twenty-eight years, had suffered with chronic diarrhœa for five years, the dejecta containing blood and pus. There was slight tenderness along the course of the colon; the rectum was free from trouble. No amœbæ were found in the stools. Despite careful diet and irrigations there was no essential improvement. In March, 1901, a fecal fistula was made by Steiner. The small intestine was found to be normal in appearance. The serosa of the colon, however, as far as could be examined, showed spots of thickening in various places. After the operation the feces for a time appeared both through the fistula and per rectum, but after several weeks the rectal movements entirely ceased. Irrigations daily, and then every other day, with solutions of nitrate of silver, and later with iodine, were given. Improvement was steady, but slow. Constant examinations of the centrifugalized sediment of the irrigating fluid were made, and as late as seven months after the operation a reaction for blood was found, as well as Charcot-Leyden crystals. When, finally, a year after the operation, all these abnormal substances had disappeared, the fecal fistula was closed. Nine months later the patient remained entirely well excepting for slight constipation.

The Complications and Sequelæ of Pertussis.—Robertson (*Scottish Medical and Surgical Journal*, June, 1903, p. 485) discusses at considerable length the complications and sequelæ of whooping-cough, showing that this is not such an innocent disease as it is generally held to be. Of the pulmonary complications, bronchopneumonia is probably the commonest. Em-

physema, of the alveolar type, is almost invariably present to a slight degree. It may, however, be of the interstitial type, involving the mediastinal tissues and spreading to the cellular tissues of the neck, and eventually infiltrating the subcutaneous tissue of the whole body. Pneumothorax from rupture of distended alveoli has occurred. Owing to weakening of the bronchial walls bronchiectasis has resulted.

The nervous complications are varied and not infrequently rather serious. Convulsions are the most frequent, and usually occur during a spasmodic attack. Whereas these are usually believed to be due to cerebral congestion, Robertson is rather inclined to think that they are due to the degree of extreme nerve irritability induced by the action of the specific toxins on the nerve cells of the motor cortex. The paralyses that occur are of great interest and are not rare. They may come on during the spasmodic stage or in convalescence. That some of these, occurring in the acute stages of the disease, are due to submeningeal hemorrhages has been demonstrated by autopsy. Those occurring in convalescence are probably the result of the effect of the toxins on the bloodvessels or nerve cells. The hemiplegias which occur may be due either to submeningeal or intracerebral hemorrhage. Thrombosis of the cerebral vessels has been described. Valentine has analyzed 83 cases of paralysis occurring after pertussis. Of these 62, or 74.6 per cent., were of cerebral origin. Of the cerebral cases 40 were cases of hemiplegia (21 were right-sided, 15 left-sided, and in 4 the side was not mentioned); 16 were cases of monoplegia affecting the function of the arm, face, or leg, or of speech or sight; the remainder were paraplegias. The prognosis was not very good, as only about 40 per cent. of the paralyses were recovered from. Alexander Bruce reported two cases of spastic paraplegia following whooping-cough, and Foggie has recently recorded a case where cerebral diplegia followed the disease. Localized paralyses, involving various of the cerebral nerves, may occur. Möbius has described a case of ascending paralysis of the spinal cord following pertussis in a child aged three years.

Of the circulatory disturbances dilatation of the heart is the most frequent and serious. If there be any previous weakness of the heart muscle, it may be the cause of a fatal result.

Knight found albuminuria in 66 out of 86 cases examined. It is usually present in mere traces. In about one-fifth of the cases of albuminuria blood cells are present, and in a few hyaline casts are also found. Non-diabetic glycosuria is not an infrequent accompaniment, especially in the cases accompanied by convulsions.

Transient loss of vision is said by the writer to be a frequent complication. In most cases this is due to a disturbance of the cerebral circulation, but it may be due to a retinal hemorrhage. Subconjunctival hemorrhages are common. Strabismus, both temporary or permanent, may occur. The membrana tympani has been ruptured during an attack of coughing.

Some Points on Metabolism in Gout, with Special Reference to the Relationship between the Uric Acid and Phosphoric Acid Elimination in the Intervals and during Acute Attacks.—FUTCHER (*The Practitioner*, August, 1903, p. 181) points out that there is some theoretical basis for the

opinion that there might be a parallel relationship between the uric acid and phosphoric acid excretion in gout. Both are products of the disintegration of nuclein. Nuclein breaks up into albumin and nucleinic acid. Nucleinic acid further disintegrates into phosphoric acid and a so-called "mother substance." This "mother substance" yields both xanthin bases and uric acid, the amount of each depending upon the conditions favoring oxidation.

The excretion of uric acid and phosphoric acid was followed in a number of gout cases during the acute attacks and in the intervals. The investigation seemed to show a close parallel relationship between the two. In the quiescent intervals both were markedly below normal. Two or three days after the acute arthritic symptoms commence the phosphoric acid and uric acid gradually increase until they reach the average normal output, or even the upper limit for normal. As the acute manifestations subside, both steadily fall and remain below the lower limit for normal until the onset of the next acute attack. The investigation pointed strongly in favor of the view that both are products of nuclein disintegration.

The Diet in Nephritis.—KOESTER, of Gothenburg (*Nord. medizin. Archiv Jarg.*, 1903, Abt. II., Anhang, 138), has carefully studied a number of patients with different forms of nephritis under four different diet régimes, which were varied from time to time with each patient. These diets were (1) an exclusively milk diet, one and a half litres a day; (2) milk and vegetable diet; (3) white meat and eggs; (4) ordinary mixed diet.

The results of his observations the author shows in instructive tables. The following conclusions were reached:

1. In acute nephritis a strict milk diet is indicated, and only after the disappearance of the acute process should this be changed.

2. The same holds for acute exacerbations in chronic nephritis.

3. It is best to begin the treatment of a chronic nephritis with a strict milk or milk and vegetable diet. When, however, the excretion of albumin during this treatment becomes for some time constant in quantity, then the patient may without danger be allowed a more mixed diet, even with meat of any kind.

4. Œdema and ascites are no contraindications to a mixed diet if the patients desire it.

5. It is a matter of indifference whether the patient be given red or white meat. Alcoholic liquors and condiments are contraindicated. It is often of advantage, after a diet containing meat has been continued for some time, to order for a short time a strict milk diet. During this treatment a diminution in the excretion of albumin may come about, which later continues.

In the discussion Aaser, of Christiania, agreed with Koester that a strict milk diet in chronic nephritis was not only unnecessary, but might be even dangerous. He had seen patients improve when a milk diet was changed for a mixed diet. Even in acute nephritis, after scarlet fever and diphtheria, the author believed that sometimes a mixed diet, consisting in the main of milk, bread and butter, and fish, was of advantage. Sometimes in mild cases a little meat even is allowed. In none of his cases in which this diet

had been allowed had uræmia come on, while he had often seen this occur under an exclusively milk diet. Our knowledge concerning the effect of the diet in nephritis is very slight.

Laache, of Christiania, agreed entirely with the conclusions of Koester. One should not be too strict in the diet in chronic conditions. There are cases of individuals with chronic albuminuria who lie in bed of their own accord for weeks and months on a strict milk diet; but, though the albumin may sometimes disappear, it usually soon returns at the end of the treatment. In acute nephritis, however, he believes that it is unwise to deviate from the generally accepted diet, namely, one consisting mainly of milk, together with easily digested carbohydrates.

Sivén, of Helsingfors, calls attention to the fact that, recognizing that the final product of the digestion of albumins—in the main, urea—is excreted through the kidneys, while those of the cholehydrates and fats are excreted mainly through the lungs and skin, we seek to give a diet which contains as little albuminoid material as possible. A milk diet is, however, scarcely rational, inasmuch as the quantity of milk sufficient for the nourishment of an adult (three to four litres a day) contains 105 to 140 grammes of albumin, or as much as an ordinary man takes daily in his usual diet. One would then scarcely expect a better result from a milk diet than from an ordinary mixed diet, a fact which appears to be demonstrated by Koester's interesting investigation. The main difference between a milk diet and the ordinary diet is that the latter contains a mass of extractives (purin bodies, etc.), concerning the influence of which upon the kidneys but little is known. He is inclined to believe that the fears of possible harm from a diet containing a minimum amount of albumin are exaggerated, and believes that it would be practical and advisable to test the effect on nephritis of a diet consisting solely of carbohydrates and fats.

The Discovery of the Cause of Sleeping Sickness.—An extremely important discovery has been made by CASTELLANI, of Florence (*Lancet*, London, 1903, vol. ii. p. 1735), who, while engaged in a study of the problematical sleeping sickness of Africa, has found in the cerebrospinal fluid of cases of this disease, obtained by lumbar puncture, living trypanosomes. They are not found in large numbers, and it is necessary to draw off at least 15 c.cm. of the cerebrospinal fluid. "It is better to reject the first few cubic centimetres, as they are apt to contain blood." As soon as the fluid becomes clear 10 c.cm. are collected, and after centrifugalization there is found at the bottom a slight whitish sediment and in some cases a minute trace of blood. If the liquid above the sediment be poured off, a moderately low power of the microscope reveals the trypanosomes. These have been found during life in twenty out of thirty-four cases of sleeping sickness. On two occasions they were also found in fluid from the lateral ventricles, and in one instance in the blood. The author does not believe that the trypanosomes result from the admixture of blood, as in cases where no trace of blood was found the trypanosomes have also been present. In twelve cases of other disease the cerebrospinal fluid was free from these organisms, although several of the cases were instances of ordinary trypanosoma fever, cases which have no clinical similarity with sleeping sickness. The organisms found differ, as far as the author has been able to observe, in no way from the species found

in the blood of trypanosoma fever—T. gambieuse (Dutton)—though, as a rule, the micronucleus lies nearer the extremity, and the vacuole is apparently larger. In post-mortem examinations of 80 per cent. of the cases where the trypanosoma was found during life, the author cultivated from the blood of the heart and from the liquid of the lateral ventricles a streptococcus which he has already described. He believes that this represents a terminal infection.

As a note to this article the Secretary of the Royal Society, Prof. Foster, states that Bruce, who is now continuing these observations, has found the trypanosoma in the spinal fluid in every one of thirty-eight cases of sleeping sickness, and in the blood of twelve out of thirteen cases.

The Contagiousness of Scarlet Fever.—The old idea that contagion in scarlet fever is chiefly conveyed by the exfoliating skin has of recent years been brought into considerable doubt. Most interesting observations on this point are communicated by AASER, of Christiania (*Nord. med. Arch.*, 1903, Abt. II., Anhang 51). From 1895 up to June, 1902, Aaser had under his care 3800 cases of scarlet fever, 79 of which obtained their infection from patients who had been discharged from the hospital as well and were supposed to be free from the contagium. The average length of time during which these individuals had been under hospital treatment was nine weeks. The patients were all most carefully washed and disinfected, and the boys' heads were all shaved and scrubbed before discharge. Of these patients 40 were boys and 39 girls, so that sex apparently played no important rôle. That the hair played no part in conveying the infection would apparently be shown by the relation between the number of boys and girls in this group of cases. In 38 per cent. desquamation had entirely ceased one week before discharge, and in the rest from one and a half to four or five weeks. The author believes that too much weight had been laid upon the importance of desquamating epithelium, asserting that in many instances children freely desquamating have failed to convey the disease to susceptible individuals. He is convinced, at all events, that in these cases the transmission of the disease could not be ascribed to desquamation. On careful analysis of his observations, however, the result of which is shown in an excellent table, he has become convinced that the main source of infection was the presence of some local affection of the throat, nose, or ear, associated with discharge. In conclusion he says: "My observations show that some patients with scarlet fever may remain sources of contagion for a time far behind the usually recognized period. They show, further, that the termination of desquamation is of itself no criterion as to how long contagiousness remains. The poison can apparently remain for a considerable length of time in the nose, throat, and middle ear. Through the secretion from these mucous membranes the poison is further distributed. In this secretion, then, lies the danger of infection.

"As long as there is an abnormal secretion the patient must, therefore, remain isolated, even if the period be twice as long as is ordinarily regarded as necessary, and the patient with scarlet fever should never be discharged until the physician has convinced himself by careful examination of the throat and nose (anterior and posterior rhinoscopy) that the secretion had ceased."

SURGERY.

UNDER THE CHARGE OF

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Multiple Chancres.—PIERRON (*Archives de méd. et de pharmacie militaires*, No. 2, 1903) reports the interesting case of a man who presented himself for treatment with six distinct and separate chancres on the penis. The secondaries were slight and the severity of the case seemed in no way to be proportionate to the number of the chancres, and the disease ran a mild course and responded favorably to specific treatment.

Three Successful Laparotomies for Intestinal Perforation in Typhoid Fever.—HARTE (*Annals of Surgery*, July, 1903), after reporting three successful cases, states that the keynote of success in dealing successfully with this condition is the early recognition of the lesion. At the best this is a most difficult procedure and the diagnosis can best be made by the medical attendant who has carefully followed the case from the beginning, noticing all the trifling changes that occur in the abdomen. When any undue symptom arises the surgeon should be immediately consulted. The classic symptoms of perforation, when well marked, can hardly be mistaken—such as pain, tenderness, rigidity, shock, chill, facial expression, and all the symptoms of peritonitis. Muscular rigidity is one of the earliest and most important signs of intraperitoneal irritation. The leukocyte count has proved of very little value at the time when most needed. Immediate operation should be urged even in the presence of profound shock, as every hour of delay proportionately decreases the chances of recovery. In 332 reported cases a median incision was made in 96, with a mortality of 78.12 per cent.; in 123 cases a right lateral incision was made, with a mortality of 68.37 per cent., while in the other cases operated upon the site of the incision was not mentioned. When the perforation has been found, and its closure will not produce too great stenosis of the bowel, it should be rapidly closed with silk sutures in whichever direction, either transversely or longitudinally, to the lumen of the bowel which produces the least narrowing of the gut. No time should be wasted in attempting to trim or freshen the edges of the ulcer. The best stitch is the so-called mattress suture, as a running Lembert is apt to cut or tear through the friable tissues. When the opening is closed the bowel should be carefully inspected for other perforations, as not infrequently these openings are multiple. Often dark necrotic spots are found where the ulcer has destroyed the coats of the bowel down to the peritoneum. These

should be treated just as though a perforation had taken place and the weakened area fortified by being folded in with stitches.

When closure is not practicable by means of the opening being too large or the area of inflammation too great, one has the choice of four procedures: (1) A plug of omentum may be fashioned and stitched against the opening in the bowel so as to form a simple patch, after the manner in which nature sometimes deals with these conditions. (2) Resection of the bowel and an end-to-end anastomosis either with stitches or a Murphy button, the latter being much more rapid. (3) The formation of an artificial anus by stitching the bowel to the abdominal wall, and (4) cutting off the damaged area of the bowel from the general peritoneal cavity by carefully placing pieces of gauze between the folds of the bowel. The peritoneal cavity should be thoroughly cleansed with salt solutions and ample provision made for drainage. Little or no attempt should be made to close the abdominal wound. In conclusion the author states that there are two important factors to be carefully considered. First, the early recognition of the lesion and dealing with it as rapidly as possible, in order that as little time as possible will elapse from the time of perforation until operation has been performed; and, second, that the operation should be so planned, since time is so important an element, that not a moment should be wasted during it, the technique being of the simplest character, as every moment of delay will cause a much higher percentage of mortality.

THERAPEUTICS.

UNDER THE CHARGE OF

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Diet in Gout.—SIR DYCE DUCKWORTH (*Practitioner*, July, 1903) says that with regard to animal food generally, it is not only harmless, but beneficial to gouty persons provided it be taken in moderation. The alleged difference between red and white meats he regards as nonsense. Tender mutton is, of course, more digestible than tough beef. He recognizes no differences between red and white meats and fowl and any variety of game in regard to gout-provoking qualities, provided the quantity consumed is restricted and the cooking is plain and appropriate. Fish is one of the best articles of diet for the gouty. Lobsters, oysters, and most shell-fish are quite innocuous provided they are eaten fresh. No viscera, such as heart, liver, sweetbreads, etc., need be excluded from the diet.

With reference to vegetable food, ordinary bread, plain or toasted, or plain biscuits, are, of course, permissible. He finds it hard to understand why potatoes should have ever been forbidden; plainly cooked, they are quite harmless. The assertion that roots and vegetables grown underground are harmful he says is rubbish, and fruit is condemned on very inadequate grounds. Most gouty persons can take fruit cooked or raw in moderation, not only with impunity, but with benefit. Tea, coffee, and cocoa are quite harmless. Sugar taken in moderation is not only harmless, but beneficial. Wines and alcoholic liquors require much discrimination. Many gouty persons are best without any, but the fact remains that many others are better for the use of a little good wine taken with one meal in the day. There can be no universal rule as to kind or amount. Most varieties of malt liquors are harmful to the majority of gouty patients, but in summer many persons can take small quantities of the lighter varieties, such as beer, with impunity and benefit. Well-prepared cider is an excellent drink in warm weather for gouty patients, but the quantity should not exceed a pint. He lays great stress on individualizing in cases of gout, and says that curtailing the food and sending patients away to spas is generally harmful.

Treatment of Gout.—Dr. Arthur P. Luff (*Practitioner*, July, 1903) says that gout is a disease that is due to faulty metabolism, probably both intestinal and hepatic, as a result of which certain poisons ("possibly the purins and other bodies, but of which we at present know but very little, lead to autointoxication, which is an early factor in the development of the gouty condition"). He thinks that with increasing knowledge and experience of the disease uric acid and its salts will in all probability have to be relegated to a position of subsidiary importance in the pathogenesis of gout. The joint manifestations are probably dependent upon much more general and much larger conditions than a mere excess of uric acid in the blood. The deposition of sodium biurate is possibly merely the sign of the disease, not the essence of it.

As regards the treatment of gout, he said that it should be borne in mind that no routine line can be laid down that can be adopted suitably to all cases. Individualism—the treatment of the patient rather than the disease—is the prime feature. The treatment of gout, in his mind, should have for its aim the following objects:

(1) The treatment of the gouty paroxysm in cases of acute gout, and the relief of pain as speedily as possible; (2) the treatment of the subacute or chronic condition and the prevention of the recurrence of an attack, which may be effected by the promotion of the elimination of the uric acid and the other purin bodies, by checking any excessive formation of these bodies that occurs in some subjects, and by careful attention to diet and general hygiene; and (3) the treatment of the affected joint or joints with the object of removing the uratic deposits and of preventing permanent deformity. For the treatment of the gouty paroxysm the limb should be placed in the horizontal position, or slightly elevated above the level of the body, and a cradle should be arranged so as to take the weight of the bed-clothes off the affected part. To alleviate the severe pain felt in the affected joint warm-packs should be arranged around it, consisting of cotton-wool saturated with a soothing

lotion, and then lightly covered with oiled silk. He has found the following lotion most useful in relieving the local pain:

℞.—Sodii carb.	. . . . .	℥iv.
Linim. belladonnæ	. . . . .	℥ij.
Tinct. opii	. . . . .	℥iss.
Aq.	. . . . . ad	℥viij.

A small portion of the lotion should be mixed with an equal quantity of water, and then poured on the cotton-wool previously arranged around the joint. The pack should be changed every four hours. In connection with the acute paroxysm no attempt at local depletion—such as the application of leeches to the inflamed joint, blistering, or incisions—should on any account be made, owing to the liability of thereby extending the inflammatory condition, and so producing subsequent ankylosis or deformity.

For the internal treatment of acute gout colchicum is one of the most valuable of drugs. It should be especially used for acute gout and for subacute attacks supervening on chronic gout. If it be used continuously, tolerance is apt to be acquired, and the drug ceases to act. At the commencement a large dose of 30 or 40 minims of the wine with from 40 to 60 grains of citrate of potassium should be administered three times a day. The citrate of potassium, which is given for its combined properties of acting as a diuretic and of diminishing the acidity of the urine, may, if desired, be given as an effervescing mixture, using 30 grains of potassium bicarbonate to 20 grains of citric acid. Colchicum reduces the gouty inflammation, relieves the pain, and shortens the attack. It should only be taken under medical advice, and should never be given in such doses as to produce extreme depression. After the inflammation of an acute attack has subsided the doses of colchicum should be diminished until it is left off. From 3 to 4 grains of "blue pills" should be given the first night, followed by a dose of Epsom salts in the morning. Mercury should be given only in sufficient doses to produce its cholagogue effect, as owing to the possibly defective action of the kidneys the mercury absorbed into the general system may be eliminated with great difficulty. In his opinion it is advisable in the treatment of gouty patients in the acute or subacute stages to avoid the use of saline purgatives owing their efficacy to salts of sodium, on account of the power possessed by all sodium salts of diminishing the solubility of sodium biurate. In the employment of purgatives for gouty patients the great object is not to produce powerful purgation, but to relieve portal congestion, since a congested condition of the liver means that excessive quantities of glycogen and purin bodies remain in the circulation, with the consequent production of an excessive quantity of uric acid. A pill containing either 2 grains of euonymin or ¼ of a grain of podophyllin, combined with 1 grain of extract of hyoscyamus and 1½ grains of the compound extract of colocynth, will in many cases be found to be very useful.

If the pain of an acute attack of gout is so severe as to prevent sleep, chloral, sulphonal, or trional may be given, or a full dose of extract of hyoscyamus given with blue pill at night will in some cases act as a very useful anodyne. The administration of opium or morphine should, if possible, be avoided, owing to the risk of its deficient elimination, and also on

account of its diminishing the amount of urine, and its tendency to derange digestion and check hepatic metabolism.

The means of checking the excessive formation of the purin bodies consist in careful attention to diet and regimen, in the production of the metabolism of the liver, so as to check the excessive production of the antecedents of uric acid, and in the relief of congestion of the portal system, which can be effected by keeping the bowels open at least once a day. In addition to colchicum, which may be given in small doses, guaiacum may very usefully be administered as an alterative, which stimulates the metabolism of the liver and also affords relief to the portal system. From 5 to 10 grains of guaiacum resin should be given in cachets two or three times a day, according to the effect on the bowels, since guaiacum sometimes acts as a laxative. The method of administering the powdered guaiacum resin in cachets is far preferable to giving the tincture of guaiacum in a mixture, as in the latter form a nauseous mixture is produced and the precipitated resin tends to cling obstinately to the tongue and fauces. In cases of chronic gout the colchicum may very conveniently be administered in the form of a pill, given three times a day, containing $\frac{1}{60}$ of a grain of colchicine, combined with $\frac{1}{4}$ of a grain of extract of nux vomica and 1 grain of extract of gentian. Colchicine, however, should not be given in cases of marked interstitial nephritis, as in such cases a fatal result has been known to follow its administration in medicinal doses. If constipation occur a sulphur and guaiacum tablet or a dose of compound licorice powder should be administered at night. An occasional dose of blue pill and euonymin, followed by a purge of Epsom salts, will be found useful. If the patient is suffering from atony and debility of the stomach nux vomica or strychnine may be given with potassium citrate. Iron preparations are not, as a rule, well tolerated by the gouty, but if anæmia is present the citrate of iron and ammonium or the carbonate of iron will be found the best to administer. Regarding the use of alkalies and the salts of alkalies, he says that of the potassium salts used in the treatment of gout the citrate and the bicarbonate are the two most commonly employed. As to the beneficial effects of employing a potassium salt in conjunction with colchicum in the treatment of acute and subacute gout he is fully assured, and he has found that of the various potassium salts the citrate is the most useful. If given in sufficiently large doses it tends, by its conversion in the kidneys into the carbonate, to diminish the acidity of the urine, which is generally high in connection with the gouty paroxysm, while at the same time it increases the solvent power of the urine for the uric acid salts, and so assists their elimination. In addition, as he has experimentally shown, the presence of a potassium salt both delays and inhibits the conversion of the soluble gelatinous sodium biurate, which is the form in which the biurate is first present in the blood, into the comparatively insoluble crystalline biurate. In this way the deposition of the latter in the tissues is inhibited, and so further time for the elimination of the biurate is offered. He does not, however, wish to contend that the above-mentioned are the only explanations of the beneficial action of potassium salts in the treatment of gout. In addition, they have their uses in the gouty state on account of their stimulating action on metabolism, of their remedial action on the gastric and hepatic functions, and

of their diuretic effect. As regards the use of sodium salts, they are certainly beneficial in some gouty conditions, but since they are directly detrimental to the removal of gouty deposits, he is of the opinion that those mineral waters should be avoided which owe their activity to those salts when the removal of gouty deposits is the main object of treatment. But in cases of sluggish action of the liver, of gastrointestinal catarrh and torpor, of gouty dyspepsia, and of other forms of irregular gout where there are no appreciable uratic deposits in the joints, mineral waters containing sodium salts are undoubtedly beneficial, owing to the action of those salts as hepatic and gastrointestinal stimulants. As regards the use of lithium salts in the treatment of gout, his opinion is that they are not so useful as the potassium and sodium salts. The lithium salts have not the same inhibiting effect on the conversion of gelatinous sodium biurate into the crystalline form as the potassium salts have, while at the same time they have no better solvent effect on gouty deposits. The great objections, however, to the use of the lithium salts is their greater toxicity and depressing action on the heart as compared with the potassium salts. They consequently have to be given in very small doses, and thus he is very doubtful as to whether in such doses they possess any remedial effect at all. On the other hand, he frequently meets with patients suffering from cardiac depression as the result of the excessive and continued consumption of lithia tablets, which are so persistently, so speciously, and so wrongly vaunted as curative of gout. Cataphoresis is useful in many cases of chronic gout with considerable deposits in the joints, and also in many cases of obstinate rheumatoid arthritis.

As far as the preventive treatment of gout is concerned, Dr. Luff has now had a considerable experience of the prophylactic effects of guaiacum resin, and he says that he knows of no drug that is more useful in the preventive treatment of gout. Its action is probably due to its stimulating effect on hepatic metabolism, thereby increasing, as it undoubtedly does, the elimination of uric acid. The form in which he prefers to give it is that of the powdered resin in cachets, commencing with doses of 5 grains three times a day after meals, and gradually increasing the dose to one of 10 or 12 grains. In this form it can be taken without any discomfort to the patient, whereas if administered in the form of the tincture in a mixture a most nauseous medicine results. Quinic acid is a comparatively new drug, which in various forms of combination has been put forward as possessing some beneficial action in the treatment of gout. It diminishes the output of uric acid in the urine, but simultaneously increases the secretion of hippuric acid. His experience of the different combinations of quinic acid is somewhat limited, but so far he is inclined to think that they are of decided use in the treatment of certain forms of chronic gout. The administration of fruits frequently reduces uric acid excretion, a result which has been attributed to the effect of quinic acid. Gowland Hopkins considers that this diminution is due to interruption of some synthetic process rather than to a mere effect on excretion.

The diet of gouty patients should be simple, that is, the meals should not be made up of too many articles. Simplicity of food means facility of digestion. Certainly meat, even red meat, should not be excluded from the diet. No class of food-stuff is so productive in energy as animal food; and as most

cases of chronic gout are suffering from lowered vitality and want of tone, animal food, at all events in moderate quantity, is distinctly indicated. The author's experience supports the truth of this view, as he has advised in the great majority of cases of chronic gout the taking of at least one meat meal a day. The exclusion of any article of diet or of any class of food without taking into account the surroundings of the case and the peculiarities of the individual is unscientific. The value of a given mineral water in the treatment of gout depends greatly on the main object with which it is taken. For instance, it may be taken to remove gouty deposits, or to stimulate the action of a sluggish liver and to relieve portal congestion, or for the treatment of gouty dyspepsia, or to relieve the bowels in cases of torpor and gastrointestinal catarrh, or to act on the kidneys, or to relieve gouty affections of the skin. Now it is manifest that any one mineral water is not likely to produce all these effects, and it is also obviously conceivable that a mineral water which might be most useful to effect one of these purposes might prove most injurious if employed to effect another. No doubt considerable error has arisen from indiscriminately sending gouty patients to a particular spa without giving due consideration to the question as to whether the water of that spa is suitable for the treatment of the specific gouty disorder from which the patient is suffering. Moreover, it is well to bear in mind that a patient should not be sent to a spa during the acute stage of gout, nor if suffering from marked organic disease of the heart or kidneys. A fairly bracing air with a low relative humidity is, in the experience of the author, the most suitable for the gouty. High mountain situations and valleys where there is an excessive relative humidity of the air are alike unsuited to the gouty. Especially is it desirable to avoid exposure to the cold east and northeast winds which prevail in this country in the early months of spring, and which are so apt to be provocative of what has been called a "chill on the liver," a condition which no doubt is brought about by the chilling effects of these winds on the skin, and a consequent reflex affection of the metabolism of the liver cells. As a winter resort for the gouty he knows of no better climate than that of Egypt, where, at Helwan (Helouan), thermal, sulphurous, and saline waters exist, and excellent baths are obtainable. The air of Helwan is that of the desert; the average winter temperature is 60° F.; the relative humidity from November to April is only 30 to 60 per cent., while the average rainfall for four consecutive winters was only three-quarters of an inch. For the spring, summer, and autumn months we fortunately have for our selection a large number of health resorts in this country and on the Continent, the climates of which are well suited to the gouty. The author's experience is that residence by the sea is not suited to most cases of gout, and this especially applies to cases of gouty eczema.

Blood-letting in Uræmia.—Dr. M. Jaerisch (*Münchener med. Wochenschrift*, 1903, vol. xxix., No. 13, p. 232) communicates an observation on a young girl of seventeen years who had acute nephritis of unknown origin. Nothwithstanding careful medication, the patient was attacked with grave uræmic convulsions, there occurring between seven o'clock in the evening and five o'clock in the morning no less than forty-seven crises. She was promptly bled; 500 grams of blood were taken from her, followed by the

injection of a physiological saline solution. The patient did not recover until the second bleeding of 500 grams had taken place, following which the pulse rate became better and the convulsions diminished, and in a few days the patient had recovered.

Alcohol and Bacteriolysis.—DR. H. A. HARE (*Therapeutic Gazette*, 1908, vol. xix., No. 5, p. 239) gives some interesting experiments to determine whether alcohol does good in infectious disease by increasing the bacteriolytic power of the blood, a subject which has been very much agitated in foreign laboratories. In these experiments, closely following out many others of the Continental workers, he comes to the following: (1) The conclusions to be reached from this research are that the use of alcohol seems to have the power of combating infectious diseases by increasing the bacteria-destroying power of the blood; (2) while the experiments so far made are too few and too contradictory to determine the question, they indicate so far as they have gone that this effect is produced, to some extent at least, by an increase in the complement.

GYNECOLOGY.

UNDER THE CHARGE OF

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ASSISTED BY

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Acute Diffuse Peritonitis.—LENNANDER (*Deutsche Zeitschrift f. Chirurgie*, Band lxii., Heft 1 und 2) recommends, during the early stage, the entire withholding of food by mouth, hypodermoclysis and ice-bags. Later he gives saline enemata and rectal alimentation with the subcutaneous use of olive oil.

Operative intervention is recommended when there is no evidence of gradual improvement, or if there is reason to suspect perforation of a viscus or pus sac. If pus is localized it should be mopped out with dry gauze, without irrigation, and a gauze drain inserted. The abdomen may be opened under local or light general anæsthesia and drained at the most dependent points, per vaginam, if there are pus foci in the pelvis. The writer is opposed to irrigation of the abdominal cavity in diffuse peritonitis unless it is impossible to dry it thoroughly and there is no danger of infecting healthy surfaces.

Tympanites is treated by puncture or incision of the gut. Intestinal paralysis may require the establishment of a fecal fistula. The after-treatment consists in frequent change of dressings, laxatives, nutrient enemata, and the subcutaneous injection of oil, saline or grape-sugar solution (5 to 10 per cent.).

FRIEDRICH (*Archiv f. klin. Chirurgie*, Band lxviii., Heft 2) found in cases of diffuse peritonitis numerous anaërobic bacteria, which produce dangerous toxins that exert an intense transient local irritation, varying with the amount of poison which is developed.

The essential point in the treatment is to open the abdomen in order to favor aërobiosis, while the introduction of saline solution into the circulation both assists the elimination of the toxins and at the same time strengthens the heart action. Subcutaneous injections of grape-sugar (3 to 5 per cent. solution) increase osmosis as well as supply nourishment. The writer has used hypodermically from one to three ounces of olive oil daily. In operating he seeks to remove the primary focus of infection and then to drain freely in all directions when there are extensive exudates. He saved seven out of nine cases of diffuse peritonitis following perforation of the appendix, but all the others died.

Changes in the Ovaries in Cases of Vesicular Mole.—PICK (*Zentralblatt f. Gynäkologie*, 1903, No. 34) reviews the literature of this subject thoroughly and adds the report of an interesting case. He agrees essentially with Stoeckel, inferring that in cases of vesicular mole and epithelioma of the chorion changes occur uniformly in the ovaries—polycystic lutein degeneration or general overproduction of lutein.

Menstruation and the Corpus Luteum.—LINDENTHAL (*Wiener klin. Wochenschrift*, 1903, No. 11) believes that the amenorrhœa sometimes observed after the extirpation of one ovary is due to the fact that the ripe follicle, the bursting of which would have caused the menstrual flow, was removed. This view, he thinks, is supported by the well-known fact that menstruation is often delayed for seven or eight weeks after unilateral oöphorectomy. In other words, it is not always true that the remaining ovary at once assumes the functions of the one which has been removed.

In order that menstruation may proceed regularly, it is necessary not only that Graafian follicles should be present, but that they should rupture every month and form corpora lutea. As long as no corpora lutea are formed, the genital organs remain undeveloped, and after their formation ceases the menstrual flow ceases and retrograde changes occur, though the ovary may contain follicles both before and after the period of sexual activity.

Hæmatocele Not Always Evidence of Ectopic Gestation.—SCHAMBACHER (*Zentralblatt f. Gynäkologie*, 1903, No. 36) calls attention to the fact that the mere presence of pelvic hæmatocele is not in itself a proof of the existence of extra-uterine pregnancy, in the absence of microscopic evidence. He believes that many cases of pure hæmatosalpinx are mistaken for ectopia in the absence of a careful examination of the blood as well as of the tube for chorionic remains.

Tuberculous Infection of Ovarian Cysts.—PRÜSMANN (*Archiv f. Gynäkologie*, Band lxviii., Heft 3) reports a case, and cites twelve others from the literature. In his case the inner wall of the cyst was studded with tubercles containing typical bacilli. No evidence of tubercular nodules or infiltration

was found in the fibrous or serous layers or in the corresponding tube. In the broad ligament near the pedicle there were collections of leukocytes in the lymphatics, with giant cells. The writer infers that in this and in similar cases there is a secondary invasion of bacilli into the main cyst, usually from the infected tube, gut, or peritoneum. In all except the writer's case and one other the peritoneum was tuberculous. He infers that in his case infection occurred from the vagina through the lymph channels, possibly during coitus.

Epithelioma of the Chorion.—FLEISCHMANN (*Monatsschrift f. Geb. u. Gyn.*, Band xvii., Heft. 1) reports the case of a multipara who, three years after the removal of a vesicular mole, presented herself with a tumor which grew from the uterine cavity, filling the vagina. Since hysterectomy was not permitted, the growth was removed, and nine days later the uterine cavity was curetted on account of profuse hemorrhage. A quantity of soft tissue was removed and the uterine wall was accidentally perforated. A tampon was introduced, and the patient was again urged to have total extirpation performed, but refused; and after another profuse hemorrhage, left the hospital. Three months later she appeared in good health, having had no return of the bleeding. The vaginal cicatrix was normal, the uterus (previously as large as the gravid organ at two months) was small, and the adnexa free. Ten months after operation she was again examined and all her organs were healthy. Menstruation was regular and she had gained in weight.

A careful examination of the growth confirmed the previous diagnosis of epithelioma of the chorion, made up of syncytial epithelium, with metastasis in the vagina. The writer regards the case as of unusual interest because of its slow development, the absence of hemorrhage before operation, and the perforation of the uterine wall without subsequent ill-effects. The return of the uterus to its normal size and the re-establishment of the menses and general health of the patient were equally remarkable. The case seemed to be an exception to the well-known history of these neoplasms, which have always been regarded as so malignant that a radical operation offers the only hope of cure.

Adenoma of Gartner's Duct.—MEYER (*Zentralblatt f. Gynäkologie*, 1903, No. 24) describes a congenital adenoma of the duct in an eight months' fœtus. Such growths found in the wall of the cervix uteri frequently develop from the remains of the duct, rather than from the Wolffian bodies. The writer also describes a cancerous uterus, removed at operation, in which microscopical examination showed marked glandular proliferation with transition to adenocarcinoma.

DISEASES OF THE LARYNX AND CONTIGUOUS STRUCTURES

UNDER THE CHARGE OF

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Fetid Atrophic Rhinitis.—At the recent Congress at Madrid (*Archives Internationales de Laryngologie, d'Otologie, et de Rhinologie Supplement*, May and June, 1903) DR. MOURE, of Bordeaux, recommended the attempt of distending the turbinates by interstitial injections of paraffin, which suppressed both secretion and fetor. These results are based upon the treatment of seventy typical patients by Drs. Moure and Brindel.

Nasopharyngeal Fibroma Cured by Means of Galvanocautery Puncture.—DR. URBANO MELZI, of Milan, reports (*Journal of Laryngology, Rhinology, and Otology*, August, 1903) the case of a youth, fourteen years of age, who for some years had suffered with marked disturbance of nasal respiration, together with diminution of hearing and subjective noises on the right side. This was found to be due to a fibroma occupying a large part of the rhinopharynx toward the right, blocking the right choana and covering the Eustachian outlet. Attempts were made to destroy the tumor by bipolar electrolysis, but the applications produced copious hemorrhage, and were of no avail. Electropuncture was then substituted, the platinum point being introduced through the nares, keeping as close as possible to the base of the tumor, with passage of the current at intervals for ten minutes at each sitting. After a succession of a series of sittings extending through a period of three years the last trace of the growth had disappeared.

Sarcoma in the Nasal Passage.—DR. J. PRICE-BROWN, of Toronto, Canada, reported to the Laryngological Section of the American Medical Congress at Washington (*Laryngoscope*, August, 1903) the case of a large sarcoma in the left nasal cavity of a young man twenty-one years of age. Twelve pieces of the growth were removed with either snare or scissors, and seventy-four electric cautery operations performed before its complete disappearance. The difficulties in the way of hemorrhage and other complications are detailed in the communication.

Facial Neuralgia from Antral and Nasal Disease.—At a recent meeting of the American Laryngological Association (*Laryngoscope*, August, 1903) DR. W. PEYRE-PORCHER, of Charleston, S. C., reported six cases of facial neuralgia due to disease of the nose and antrum. Some of these cases had been subjected to severe surgical procedures, including the removal of the Gasserian ganglion without permanent relief, but were eventually cured by operations upon the nose or antrum; structures which had not been

examined by any of the medical men who had had previous charge of the cases.

Inference is drawn that many cases of trigeminal neuralgia are due to lesions in the nose and maxillary sinuses, and that thorough examination of these structures should precede any resort to resection of nerve or procedure still more serious.

Lipoma of the Tonsil.—In a paper read before the American Laryngological, Rhinological, and Otological Society (*Laryngoscope*, August, 1903) DR. CLEMENT F. THEISEN, of Albany, N. Y., reports the case of a lipoma of the tonsil in a female child three years of age, and gives a résumé of a number of other instances, together with a copious bibliography. He states that there is little doubt that lipomata are due to some congenital aberration, inasmuch as the tonsil does not contain any fat. Nevertheless, he finds it rather remarkable that the majority of cases were observed in adults, the patient in one instance being a woman more than ninety years of age.

Hemorrhage following Tonsillotomy.—In an article on this subject DR. ADOLPH H. URBAN, of Buffalo, N. Y., reports (*American Medicine*, July 4, 1903) an instance in which his services were required for a lad of seven years of age, twenty-five hours after he had been operated upon for bilateral hypertrophied tonsils which had been excised without difficulty with the tonsillotome and without the use of any anæsthetic whatever. The pillars were intact, and a parenchymatous hemorrhage was seen in the left tonsillar region. Under a few whiffs of chloroform the Paquelin cautery, heated to a dull cherry red, was applied directly to the bleeding surface, and the cessation of the hemorrhage was immediate and permanent. The patient's general condition was so precarious that an infusion of normal salt solution was injected into the left median basilic vein to the amount of 700 c c. with good effect. The physician who had performed the operation had seen the patient six hours afterward, and at that time there had been neither hemorrhage nor serious symptoms of any kind.

Foreign Bodies in the Tonsil; Removal of a Bullet in the Throat Two Years after Infliction of the Wound.—DR. J. CANDEE PIERCE, of Buffalo, N. Y., reports (*American Medicine*, July 11, 1903) this curious case. A lady with an ulcer on her right tonsil applied for treatment for throat trouble of some two years' duration. On probing the ulcer a supposed calcareous deposit was struck; but noticing some powder marks on a scar of the patient's left cheek, she was asked whether she had been shot, and replied in the affirmative, stating that it was supposed that the bullet had escaped through the mouth, but she had had more or less trouble with her throat ever since. By means of knife and artery forceps the doctor then removed a 32-calibre bullet from deep behind the right tonsil.

Foreign Bodies in the Œsophagus.—DR. A. H. TRAVER, of Albany, N. Y., reports (*American Medicine*, July 11, 1903) the removal of an open safety-pin from the œsophagus of a female child nine months of age. The

pin was located by the Roentgen ray half-way down the œsophagus—too low for access by œsophagotomy. The pin was open with point upward, so that it would have been impossible to remove it through the mouth with forceps. The following procedure was adopted: "The child was anæsthetized with chloroform and placed on a table, beneath which the Roentgen-ray tube had been placed, so that the pin could be seen without difficulty. While thus keeping watch of the pin, a whalebone bougie, which could also be seen, was passed down the œsophagus until it came in contact with the safety-pin. Then, by means of the bougie, the pin was carefully pushed down into the stomach, and was seen to fall down into the cardiac end. The bougie was then removed. The child was now taken to the operating room. The abdomen was opened in the median line. The pin was located and worked up under the anterior stomach wall. An incision one-fourth of an inch long was made through the wall of the stomach and the pin removed. The incision in the stomach was closed with Lembert sutures, and the abdomen was closed in layers. The wound was dressed in the regular way. The child made an uneventful recovery, and left the hospital on the seventh day."

Retained Intubation Tubes.—For reports of some practical experiences in these cases we would refer to articles by DR. ARTHUR B. DUEL, of New York (*New York Medical Journal*, May 2, 1903) and DR. WM. T. WATSON, of Baltimore (*Maryland Medical Journal*, May, 1903).

DERMATOLOGY.

UNDER THE CHARGE OF

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Acne and its Treatment.—G. H. FOX (*Journal of Cutaneous Diseases*, March, 1903) presented an article on this subject before the American Dermatological Association, in which he states: "Of the medical treatment of acne, little need be said. A dose of salts or castor oil may often benefit the patient, but no one would be apt to speak of these as remedies for acne. In like manner calx sulphurata, ergot, glycerin, arsenic, and other drugs may, under certain conditions, prove of some service to a patient with acne, but the direct action which they produce upon an acne eruption has been greatly overrated, and their routine use by many physicians on the strength of text-book commendation is greatly to be regretted. . . . In the local treatment the best results are to be attained by measures which may be termed dynamic rather than chemical. These include massage, friction, and the use of instruments intended to empty the distended and obstructed follicles." The best instrument for general use is the curette. It is better than the lan-

cet. The author concludes by recommending "a strict diet, cold baths, systematic exercise, and the frequent use of the curette." [In the discussion of this paper certain members present were of the opinion that, while the curette might be useful in some cases, it certainly was not applicable to all, and there were other methods of treatment, both internal and local, worthy of consideration.]

Recurring Polymorphous Erythema.—GENSOLLEN (*Annales de Derm. et de Syph*, February, 1903) calls attention to this form of disease, stating that Hutchinson first, and later Bault, described such cases. Instances occurring in the practice of the reporter, as met with in Bordeaux, are next cited. There seems to be nothing remarkable about such cases, beyond the fact that the cutaneous lesions appear in recurring attacks or crops, and that each principal attack is made up of a series of successive attacks, which may last two weeks or longer. The diseases with which it is not to be confounded are (1) antipyrin erythema and (2) dermatitis herpetiformis, and it is especially from the latter disease that it must be differentiated; but dermatitis herpetiformis is altogether a more chronic process, is more polymorphous in the same attack, and is accompanied by much more itching.

Pseudoleukæmic Prurigo.—RADCLIFFE-CROCKER (*British Journal of Dermatology*, March, 1903, p. 98) reports a case of this disease in a piano finisher, aged forty-one years, apparently following a scratched finger, the wound healing rapidly, but followed a week later by a lump in the right axilla. Three months later there were several lumps as large as small eggs, with processes from them extending downward. These were extirpated, but soon afterward the glands in the left axilla enlarged, and later in the inguinal region and elsewhere. The spleen was not enlarged, the skin lesions were chiefly on the buttocks and upper half of the thighs, but also elsewhere, occurring as numerous superficial, purplish nodules the size of hempseeds and nearly all of them were excoriated from scratching, due to severe itching. The itching continued unabated until the death of the patient, about two years from the onset of the disease. The existence of severe itching in such cases, with enlargement of even a few glands, would suggest a pseudoleukæmic rather than a tubercular nature.

Four Cases of Syphilis Mistaken for Smallpox.—SCHAMBERG (*Journal of the American Medical Association*, November 29, 1902), in commenting upon such cases, states that errors of this kind are not infrequently made by physicians during epidemics and occasionally at other times, and calls attention to the points of difference in the differential diagnosis. In variola the palms and soles rarely escape, except in extremely mild cases; in syphilis these regions are seldom invaded. The syphilitic lesion possesses a firmer or harder base, and is more acuminate than the variolous, the pustulation involving the upper central portion, whereas in variola the lesions are completely involved in the pustular process and are globular and full. The course of the variolous process is rapid, while that of the syphiloderm is slow. The presence or absence of adenopathy cannot be relied upon as a diagnostic point. Most weight is to be placed upon the uniformity of the eruption and

the general symptoms in variola, and upon the crop-like appearance and the firmer, more solid base of the pustules in syphyilis.

Vaccinal Eruptions.—STELWAGON (*Journal of the American Medical Association*, November 22, 1902) states that the most notable cutaneous manifestations are of the form of erythema multiforme, urticaria, impetigo contagiosa, and pemphigoid lesions. The most generalized eruption observed was of a mixed type of urticaria and erythema multiforme—that is, a manifestation of an erythema multiforme with itching and other symptoms of urticaria. The cases of urticaria noted were marked by a disposition to the formation of vesicles and blebs; a generalized pemphigoid eruption, having the features of acute pemphigus and dermatitis herpetiformis, was observed in three instances, and having a tendency to persist over a period of months. Eczema sometimes follows vaccination, but probably only in those individuals who possess a plain tendency to eczema. On the other hand, improvement or cure of the eczema occasionally follows the vaccination. The view is expressed that psoriasis is never caused by vaccination, and that lupus, syphilis, and leprosy may be transferred by vaccination, but such instances are rare. The two latter diseases cannot be conveyed when bovine lymph is employed.

Note on the Histology of Herpes Zoster.—S. POLLITZER (*Journal of Cutaneous Medicine*, February, 1903) describes a peculiar form of vesicle in herpes zoster, which affected the mucous layer of the hair-follicle exclusively, and differed histologically from the usual vesicle as it occurs in this disease, It was a secondary effect of the real herpes zoster vesicle, which was located in the root-sheath of the hair-follicle, whence a serofibrinous exudation travelling up between the inner and the outer root-sheaths of the follicle raised up the corneous layer at the follicular orifice, producing there the visible vesicle. It is in reality herpes zoster of the hair-follicles, and has not been described before.

A Mild Inflammation of the Skin Covered by Greenish Scales, Probably Produced by B. Pyocyaneus.—M. F. ENGMAN (*British Journal of Dermatology*, April, 1903, p. 156) describes a rare case in which there existed a greenish, scaly eruption on the scrotum, the upper part of the thigh, and the perineum, chiefly on the left side. He wore a suspensory bandage, and noticed a green stain on it, which was worse when he sweated freely. B. pyocyaneus was found in the scales, so the disease was not due to malingering nor to dye in the bandage.

Case of Systemic Blastomycosis, with Cutaneous Lesions.—ORMSBY and MILLER (*Journal of Cutaneous Diseases*, March, 1903) give the result of their studies of a case in the laboratory of Drs. Hyde and Montgomery. The patient was a Swede, aged fifty-six years, a machinist, who from childhood never was robust. The first evidence of the illness which ended fatally was exhibited in the lungs. Early general toxæmia was present, as evidenced by fever, weakness, and emaciation. The cutaneous manifestations began two months after the initial illness, and were manifestly of internal origin, coming by way of the circulation. These lesions comprised subcutaneous and cutaneous nodules

and abscesses, open and discharging, or crust-covered ulcers, and were extensively distributed, being, as a rule, smaller about the head and face and larger on the extremities, the trunk having comparatively few. Pure cultures of blastomycetes were obtained from the subcutaneous abscesses before death and from various tissues and internal organs after death. Microscopic examination of both the internal and external lesions and the sputum failed to show any tubercle-bacilli, but all showed enormous numbers of blastomycetes. The lungs were riddled with miliary abscesses and tubercle-like lesions, the pleura studded with nodules, and the liver and kidneys, the spleen, and the mesentery were similarly affected. The early lung involvement and other symptoms all suggested tuberculosis, but the absence of tubercle bacilli, culturally, microscopically, and experimentally, the negative tuberculin reaction, the absence of the usual microscopic tubercular architecture, the failure to reproduce tuberculosis in animals, the extraordinary number and rapid evolution of the cutaneous lesions, and, lastly, the abundance of the blastomycetes in every lesion, ruled out tuberculosis. Photographs accompany the article.

The Light Treatment of Lupus and Rodent Ulcer.—A. J. HARRISON and W. K. WILLS (*Journal of Cutaneous Diseases*, June, 1903, p. 295) give results obtained in the Bristol General Hospital in 1901 and 1902. At first two Lorbet-Genoud lamps, made by Marshall & Woods, of London, and later two lamps made by Miller were employed. The current used was an interrupted one—5 to 10 ampères, about 12 volts, and the time of sitting at the lamps five to twenty minutes. The report covers 42 cases of lupus vulgaris, 3 of lupus erythematosus, 12 of rodent ulcer, and other miscellaneous cases. In the lupus cases almost all were benefited or greatly improved; a small percentage only were unsatisfactory. Two out of the three lupus erythematosus cases were improved, but made more rapid progress under X-ray treatment. The 12 cases of rodent ulcer were treated chiefly with X-rays and were markedly benefited.

On Light Therapeutics.—BIE (*British Journal of Dermatology*, May, 1903, p. 191, from *Wien. klin. Rundschau*, No. 37, p. 723) upholds the views of Bouchard, Widmark, and Finsen as regards the capabilities of the chemical rays, but not red, yellow, or green rays, to produce inflammation of the skin. Blue and violet rays can penetrate deeply into the skin only when it has been made bloodless. Ultra-violet rays can, under no circumstances, penetrate deeper than the superficial layer of the skin, but here they may give rise to dilatation of the vessels which can persist for five or six months. Bie gives the following conclusions: (1) Finsen's treatment of smallpox with red light depends on the exclusion of the irritating action of chemical light rays, and thus the prevention of pus-formation in the vesicles, secondary fever, and scars. (2) The red-light treatment of other exanthemata has not yet been thoroughly tested. (3) The universal light treatment of the future will undoubtedly be sun-baths or exposure of arc lamps of 150 to 200 ampères, but now too little is known of the general action of light for definite indications. (4) The single method of light treatment whose success is firmly established is Finsen's method of treating skin diseases with concentrated chemical rays.

This method is essentially preservative; hence the excellent results as to scarring, the scars being white and smooth. Healthy skin can be exposed to the rays as well as the diseased skin, thus diminishing the danger of recurrence. The treatment is free of pain and the results good. Of 640 patients, only 1.7 per cent. had to abandon treatment on account of unfavorable results; 85 per cent. showed positively favorable results; and in only 15 per cent. was the improvement so slow that the treatment had to be described as less successful.

Treatment of Rodent Ulcer by X-rays.—J. H. SEQUEIRA (*British Medical Journal*, June 6, 1903), who is in charge of the X-ray and Finsen-light Department of the London Hospital, in this article refers especially to the changes produced in the growth, the question of recurrence, the selection of cases, and the conditions which favor success. The following practical points are worthy of being quoted: The custom in the hospital is to apply the rays on alternate days in the milder cases, and daily in the severer forms of disease. The tubes used are those which spark from four to six inches, but the therapeutic value of the tubes is a variable thing, and one which it is at present impossible to explain. "High" tubes are valuable, as the rays can be applied until there is a definite inflammatory reaction. Actual "burning" is not necessary, and some of the best results are obtained without any inflammatory reaction at all. The surrounding skin is protected with leaden masks.

Electrolytic Treatment of Xanthelasma.—PANSIER (*Arch. d'Electr. Médicale*, July, 1902) recommends the use of the negative pole thrust into the growth and the application of the positive pole to the back of the neck. The patch should be transfixed by the needle. Steel needles may be used. From six to ten milliampères are employed for about two minutes. The result is a soft, non-retractile scar. The method is not painless, but this may be minimized by rubbing the eyelid with menthol and chloral hydrate, of each 46 grains in 98 grains of lanolin. Several treatments at intervals of about two weeks usually suffice.

OPHTHALMOLOGY.

UNDER THE CHARGE OF

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Cocaine. How and When to Use It in Inflammatory Affections of the Eye.—PROF. FUCHS, Vienna (*Wien. klin. Woch.*, 1902, No. 38), is convinced that this remedy is frequently improperly prescribed. It should never be

put in the hands of patients to relieve ocular pain. In fact, in conjunctival maladies the suffering as a rule is not extreme; in disease of the deeper parts, iridocyclitis, glaucoma, etc., affecting as it does but the superficial parts, it is of no value. In corneal affections the pains may indeed be often relieved by cocaine, and the physician may venture himself to make an occasional instillation; but the effect is transient, the pain quickly returns. If the patient is given the remedy he is pretty certain to use it again and again, and in that way do harm to the cornea, or at least retard healing, for it must not be forgotten that cocaine is hurtful to the cornea; it frequently causes opacities or even abrasions of the epithelium, which latter may eventuate in ulceration. It occasionally brings on an attack of glaucoma in predisposed eyes.

Prof. Fuchs employs cocaine frequently, *e. g.*, in all operations, even the least important, such as the removal of foreign bodies from the cornea. He makes several instillations of a 5 per cent. solution, and has the patient keep his eyes closed between the instillations, to obviate injury to the epithelium, which is the more likely to occur because of the desiccation that results from infrequent winking. In operations upon the lids cocaine is injected beneath the skin; in those upon the muscles beneath the conjunctiva; upon the tear passages within the same; in operating upon chalazion, besides instillation into the conjunctival sac, a couple of drops are injected into the cyst itself, rendering the curetting absolutely painless. Cocaine acts well in photophobia, as in the scrofulous ophthalmia of children, but it is not to be given to the parents. Experience teaches that the photophobia rapidly diminishes and frequently disappears in a few days if the eyes can be kept open for a little while daily. The author recommends in these cases that several instillations be made in the morning, when the photophobia is usually greatest; by this treatment the children will often keep their eyes open freely for half an hour, and this suffices to permanently relieve the photophobia to a great extent. It is often advantageous to moderate photophobia by instillation of cocaine to render possible a more careful examination of the eyes. Cocaine may be used to dilate the pupil for ophthalmoscopic examination; although not fixing the pupil, it permits pretty active contraction when the macula is brightly illuminated. Many employ cocaine and atropine in combination where dilatation of the pupil is difficult to obtain, as in severe iritis, making the instillations as often as every two hours. Fuchs is against this method. Such frequent instillations of atropine often occasion toxic effects; moreover they irritate the conjunctiva, and frequently fail of the desired effect. Under these circumstances the author recommends that atropine be used at long intervals, but in heavy doses; he recommends the insertion of a small quantity of the salt in substance in the conjunctival sac, at the same time preventing the entrance of the tears into the nose by retracting the lower lid or making pressure over the sac. This method is not to be employed in the case of little children who react so strongly to atropine. But the greatest effect is obtained from a combination of cocaine and atropine employed in the following manner: the eye is at first cocainized as preliminary to an operation, the atropine is then placed in the conjunctival sac in substance. This method of applying the mydriatic accomplishes everything that such a drug can possibly do in severe iritis, loosening old synechiæ, or freeing the iris after recent prolapse into a corneal wound or ulcer. Cocaine not being permissible

to the patient in painful ophthalmias, what is to be done? First, internal medication, *e. g.*, aspirin, which has a special advantage in iridocyclitis, and warm applications locally. A free leeching often cuts short the pain in iridocyclitis and aids mydriasis. Dionin is also to be recommended in substance or in 5 per cent. solution. A drop of cocaine previously instilled prevents the rather severe burning produced by it. Dionin sometimes causes marked inflammatory œdema of the conjunctiva. The œdema subsides in a few hours, becoming less marked the longer the drug is employed. As the reaction to this drug is somewhat uncertain, the surgeon had best make the first application himself and observe the effects. In spite of apparently augmenting the external inflammatory symptoms, dionin frequently has a happy effect in pain accompanying diseases of the cornea as well as iridocyclitis. It also exerts a beneficial influence upon the photophobia as well as the diseased processes themselves.

The Pupil in Tabes.—A. ROCHON-DUVIGNEAUD and J. HETTZ (*Arch. Gén. de Méd.*, July 7, 1903) report the results of their examination of the eyes of seventy-seven tabetics, with special reference to the reactions of the pupil. In 30 per cent. of the cases examined the Argyll-Robertson sign was incomplete; 30 per cent. of cases present bilaterally, 13 per cent. unilaterally, a complicated Argyll-Robertson sign, viz., diminution or abolition of contraction upon convergence; myosis is regularly present when the Argyll-Robertson sign is pure; optic atrophy rarely accompanies myosis; ophthalmoplegia externa or interna is even more rare; mydriasis is present only when all light perception is lost and contraction to convergence is frequently diminished or absent; when mydriasis accompanies a normal fundus, total ophthalmoplegia interna is usually present; mydriasis is most often present in those cases where the pupillary reaction to accommodation and convergence is lost, the power of accommodation being preserved.

Roentgen and Becquerel Rays in Ocular Therapeutics.—DARIER communicated to the Ophthalmological Society in Heidelberg, September, 1903 (*Woch. f. Ther. u. Hyg. d. Aug.*, Sept. 24, 1903), a series of cases treated by these rays: multiple tumors of the eyelids, conjunctiva, face, neck, and almost the entire mediastinum as far as the heart (as shown in a skiagraph). The rapid spread and the microscopic examination showed the malignant nature of the growths (alveolar round-celled sarcoma). Severe attacks of spasmodic cough with dyspnœa were endangering life. After ten ten-minute treatments by the Roentgen rays in the course of fifteen days, all the tumors of the face had disappeared. The cough and dyspnœa also vanished. The radioscope showed diminution of the mediastinal growths.

The following cases were treated with the Becquerel rays obtained from radium. These rays are known to be identical with the Roentgen rays, so that a like result is to be expected from them, with a simpler mode of application which can also be graduated: hereditary specific periorbital neuralgia with choroiditis. The pain completely disappeared after twenty-four hours' application of radium. Antipyrin, quinine, phenacetin, as well as potassium iodide and mercury, had been tried without effect. A man affected with

acute blennorrhœic iritis with severe pains had been treated without result with atropine, dionin, aspirin, and sodium salicylate. After a few hours' application of radium the pain entirely disappeared, and the pupil, which had remained contracted in spite of frequent instillations of atropine, and scopolamine (leeches had also been applied), soon dilated, showing posterior synechia. In three cases of iridocyclitis following traumatic cataract, pain was entirely relieved after a few hours, and the congestion decidedly diminished. In none of these cases was there a return of pain. In one case of old hemorrhage of the vitreous following perforating wound of the sclera, twenty-four hours' application of radium produced an extraordinary clearing up of the opacities, so that the papilla could be seen, and the vision improved from 1/10 to 1/3. Two cases of detachment of the retina and one of parenchymatous keratitis gave negative results.

Treatment of Atrophic Retinæ with Retinal Extract.—Doyne (*Brit. Med. Jour.*, July 25, 1903) reports marked improvement from the administration of extract of fresh retinæ, six to nine daily, in retinitis pigmentosa, retinal degeneration in high myopia, choroiditis, and tobacco amblyopia. He thinks that cases of asthenopia from functional exhaustion would also be benefited.

The Value of Ophthalmic Examinations in the Differential Diagnosis between Typhoid Fever and Acute Miliary Tuberculosis.—Loeb (*Arch. of Ophthal.*, September, 1903) reports a case of miliary tuberculosis diagnosed by the finding of choroidal tubercles. The patient was under his observation for three weeks, during which time the tubercles increased in size and number.

The autopsy revealed a general miliary tuberculosis. Tubercle bacilli were demonstrated in the new-growths in the eyes.

Tubercles of the choroid to be ophthalmoscopically visible must possess a diameter of more than 0.6 mm. There are usually no changes in the refractive media, and no hemorrhages. The tubercles may appear at any stage of the disease, and sometimes grow so rapidly as to become ophthalmoscopically visible over night; a second or even a third examination may be needed to demonstrate their presence. The ocular tuberculosis may be a part of a general miliary tuberculosis, or it may be the only focus demonstrable in the body.

Authorities differ as to the frequency with which tuberculosis of the choroid occurs in general miliary tuberculosis. The two extremes given are 10 per cent. and 82.7 per cent. The author thinks that we may expect to find choroidal tubercles in 50 per cent. of the cases of general miliary tuberculosis.

PATHOLOGY AND BACTERIOLOGY.

UNDER THE CHARGE OF

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Observations on the Distribution and Culture of the Chancroid Bacillus.—DAVIS (*Journal of Medical Research*, 1903, vol. ix. p. 401) has made an examination of the pus of forty cases of genital ulcerations clinically resembling chancroid. In thirty-two bacilli were found corresponding exactly in morphology and staining reactions to the Ducrey bacillus, the characteristic chain arrangement occurring in ten of these. On media containing a considerable proportion of fresh blood, pure cultures of the Ducrey bacillus were obtained directly from the pus of primary genital chancroids in two cases, and in many others there was a growth of this organism, mixed, however, with contaminating bacteria. One instance of chancroid ulceration of the skin of the abdomen, resulting from accidental autoinoculation from a genital lesion yielded pure cultures. Of seven chancroidal buboes, pure cultures were obtained in three cases. Besides the primary genital lesions, the bacillus was cultivated in pure culture from two cases of primary extragenital chancroid, the ulcerations appearing upon the fingers.

The bacillus may be identified by its morphology and staining reaction, together with its inability to grow on ordinary culture media. The growth is most luxuriant in a medium of fresh blood and bouillon, but unmixed human blood is the best medium for obtaining cultures from a source open to contamination.

A guinea-pig was inoculated by rubbing in two loopfuls of a pure twenty-four-hour culture upon a scarified area on the back, but the result was negative. Monkeys of the genus Macaccus hemestrinus were inoculated by the same method and developed definite ulcers from which the Ducrey bacillus could be isolated.

The author believes that chancroid may be primary upon an extragenital site, and that bacteriological examination of all ulcers of this type is likely to establish in the future a greater prevalence of extragenital chancroid than has hitherto been reported.—W. T. L.

On the Pathology and Bacteriology of Landry's Paralysis.—BUZZARD (*Brain*, 1903, part i. p. 94), in reviewing the pathology and bacteriology of Landry's paralysis, calls attention to the disproportion between the histological changes which can be demonstrated in the brain, cord, and peripheral nerves in certain cases and the grave clinical manifestations which characterize the disease. In a few cases no demonstrable lesions are found in the

nervous system; in a large majority of cases the lesions are such as may be produced by the action of a microbic toxin apart from the microbes themselves, and in this latter group bacteriological examinations prove negative. A few instances make up a third group in which the changes are those of a disseminated or diffuse myelitis or meningomyelitis, and in some of the cases pathogenic organisms have been found in the meninges, spinal cord, cerebrospinal fluid, and occasionally in the blood. Among the most notable observations are those of Courmont and Bonne, Roger and Josué, and Russell. These observers have demonstrated in the blood or meninges of this latter type of the disease a diplococcus which they considered bore certain resemblances to the meningococcus of Weichselbaum and to the pneumococcus. The author reports a typical case of Landry's paralysis in a man aged thirty-three years. There was a gradual ascending paralysis which lasted for about eighteen days and terminated with involvement of the respiratory muscles. At autopsy there was no noticeable alterations in the nervous system. Microscopic examination showed morbid changes of very slight degree of intensity, but of rather wide distribution, consisting principally in a chromatolysis of the ganglion cells of the anterior and posterior horns of the spinal cord. In cultures from the blood a diplococcus was isolated which stained fairly well by Gram's method. It grew slowly on the ordinary culture media. In sections of the dura mater a diplococcus could be demonstrated which resembled in morphology the coccus isolated from the blood. A subdural injection of the cultivated coccus into rabbits produced, after some days, a rapidly spreading palsy, and from the blood and dura mater of these animals the same organisms could be cultivated. The author draws attention to the unusual situation of the coccus, namely, in the dura mater, and suggests that careful bacteriological examination of this membrane should be made in cases similar to that under discussion.—W. T. L.

Experiments on Tuberculosis.—DEAN (*Journal of Pathology and Bacteriology*, 1903, vol. viii. p. 458) reports a series of interesting and careful experiments concerning the infection of animals by tubercle bacilli obtained from human sources. Observations were first made to determine whether the virulence of tubercle bacilli from the sputum of tuberculous patients could be increased for calves by an intermediate passage through pigs, cats, rabbits, and rats. The intermediate animals were inoculated with tuberculous sputum, allowed to die of the disease, and then from the most extensively affected organs the tubercle bacillus was cultivated upon artificial media. Finally, calves were inoculated subcutaneously from these cultures. Previous to the inoculations all possible precautions were taken to prevent any contamination of the calves from tuberculous cattle, and each animal received injections of tuberculin to exclude the possibility of bovine tuberculosis. After an interval of several months the calves were killed, full autopsies were performed, most of the organs were examined microscopically, and inoculation experiments made with rabbits and guinea-pigs. Of the eleven calves used, a tuberculous focus was found only in one or two. This consisted in a small, caseous nodule, which was discovered at the site of primary inoculation. Control calves inoculated directly with tuberculous

sputum developed an extensive glandular tuberculosis. The author, in explaining this apparent diminution in the virulence of the bacillus tuberculosis for the calf, emphasizes the fact that in the one case the associated organisms of the sputum had been eliminated by passage through the intermediate animals; whereas in the other case it is possible that they played an important part in aiding the attack of the tubercle bacillus. This conception was apparently strengthened by experiments upon direct inoculation of pigs with tuberculous sputum and by feeding the animals upon the material. Six pigs inoculated with tuberculous sputum developed an extensive general tuberculous infection, some dying rapidly of the disease; and three pigs fed upon tuberculous sputum, mixed with wheat meal, wasted and died, having developed tuberculosis of the tonsils and cervical glands. The author thus concludes that the pig is capable of developing a rapidly fatal general tuberculosis as the result of infection with the human tubercle bacillus.—W. T. L.

Trypanosomiasis of Horses in the Philippine Islands.—MUSGRAVE and WILLIAMSON (from the Biological Laboratory, Bureau of Government Laboratories, 1903, No. 3). The discovery of trypanosomiasis in the Philippine Islands was made by Jobling in 1901, but the first published report concerning this affection came from Smith and Kinyoun somewhat later in the same year. It is practically certain that before this time the disease did not exist in these islands, and now it is possible to trace its introduction to a shipment of horses, some of them race-horses, from Australia to Manila, in May, 1901. Since then the loss of animals from "sura" has been appalling. Trypanosomiasis, so far as is known, is a wound disease, and should the infectious agent come in contact with a wounded surface, either the skin or mucous membrane, of a susceptible animal, the disease readily develops. Proof of the transmission of the disease through biting flies has been furnished from Africa, India, and South America, and these observations have been confirmed by the authors in their investigation of the Philippine epidemic. The period during which flies are capable of transmitting the disease after feeding on infected blood appears to be less than forty-eight hours. Apparently the fly acts as a mechanical means for the spread of the disease, and not as an immediate host for trypanosoma. Since certain rats in Manila have been found to harbor the same parasite as the horse, fleas from rats may also be considered as a source of infection. The authors found it impossible to infect healthy animals by administering the blood of an infected animal mixed with food; unless abrasions were made upon the mucous surface of the mouth of the animals used for experimentation, the horses did not develop the disease. Trypanosoma are carried directly from animal to animal, and no lower form of organism is known to play the part of intermediate host. The parasite does not exist outside the animal body. The incubation period of the disease is from four to six days. After this time the temperature rises and parasites are found in the blood. The characteristic symptoms of the disease are the fever, anæmia, œdema, particularly of the hind legs, paresis, and emaciation. Early in the disease there may only be fever, and at this time a diagnosis can only be made from an examination of the blood. Later the clinical picture is typical. The course of the disease varies from two to six or eight weeks, and is always fatal in

horses. The methods which the authors suggest to rid the Philippines of the disease are the prevention of infection of the country by proper quarantine laws and the eradication of the present infection by enforcing efficient sanitary regulations.—W. T. L.

Observations upon Banti's Disease and Splenomegaly.—BORISSOWA (*Virch. Arch.*, 1903, Bd. 172, page 108) discusses the pathological changes found in Banti's disease and splenomegaly, recording two fatal cases with careful microscopic descriptions. In the first one, that of a woman, aged fifty-two years, the spleen was of an enormous size, and the general condition was complicated by a recurring ascites. At autopsy a tuberculous peritonitis obscured somewhat the pathological picture. There was no cirrhosis of the liver. The spleen, in microscopic sections, showed a widening of the blood sinuses, with proliferation of the lining endothelium, which resulted in the accumulation of great numbers of large endothelioid cells in the blood spaces. There was, besides, extensive thickening of the reticulum. Eosinophiles were quite numerous. In both the liver and bone-marrow many capillaries were found packed with large cells similar to those seen in the spleen, and the author believes that such cells were carried from the spleen to these situations by means of the blood stream.

The second case was that of an infant aged nineteen months. In the spleen much the same appearance was met with as in the first case, except that the endothelioid proliferation was not so extensive, and both red-blood corpuscles and pigment were found included in the swollen endothelial cells lining the venous spaces.—W. T. L.

The Action of the Tubercle Bacillus in Experimental Pulmonary Tuberculosis.—HERXHEIMER (*Zeigler's Beiträge*, 1903, Bd. xxxiii. p. 363) reports the results of a series of experiments in which tubercle bacilli were inoculated into the trachea of guinea-pigs. As early as one-half to one hour after the intratracheal injections tubercle bacilli were found to pass through the bronchi and bronchioli into the alveoli. During their passage through the bronchi a definite chemotactic influence was exerted upon the polymorphonuclear leukocytes which made their way through the walls of the bronchioles and eventually collected in the lumen of the bronchus about clumps of tubercle bacilli. The greatest portion of the bacilli, however, appeared to reach the alveoli without greatly damaging either the epithelium or the walls of the bronchi. In the alveoli they were immediately taken up by the alveolar epithelium, and though most of the phagocytic epithelial cells were desquamated, some still remained attached to the alveolar wall. At the same time the bacilli brought about a destruction of the elastic fibres of the lung. As a result of this damaging influence upon the stroma and parenchyma, a proliferation of the epithelium and fixed connective-tissue cells took place. The tubercle bacillus likewise caused a necrosis of the single cells, and appeared positively chemotactic for the polymorphonuclear leukocytes. The tissue about the larger collections of bacilli was entirely destroyed, and an infiltration of great numbers of polymorphonuclear leukocytes resulted. These cells, however, in their turn, rapidly degenerated. At this time giant cells appeared, more especially about the per-

iphery of the tubercle. The author traces the origin of the giant cells to the epithelioid cells, and believes that they arise as a result of a partial necrosis of the cytoplasm. Following upon the destructive properties of the multiplying tubercle bacilli, total necrosis and caseation of the tissues developed, beginning at the centre of the areas of infiltration. The author believes that though his conclusions are drawn from animal experiments, the results of his investigations are applicable to man as well as to animals.

Experimental Researches upon Cancer in Mice.—JENSEN (*Zent. f. Bakt. u. Paras.*, 1903, xxxiv. 122) reports a series of experiments made with a carcinoma obtained from a white mouse. The primary tumor had a typical carcinomatous structure, although there were no metastases. Portions of this tumor were transplanted through nineteen generations of white mice, and successful results were obtained in from 40 to 50 per cent. of the cases. The transplantations were usually made either by placing small portions of the tumor or mixtures of tumor and salt solution beneath the skin of the mice. Besides the variety of white mice in which the tumor occurred, gray mice were found to be susceptible, although in less degree; but all efforts to transfer the growth to other varieties of mice, to white rats, guinea-pigs, rabbits, and goats were unsuccessful. It appeared that the growth of the tumor in the inoculated animals was dependent upon a true transplantation, for if the tumor cells were mashed by grinding them in a mortar before the inoculations, the experiments resulted negatively. No evidence was obtained which warranted the assumption that the growth was of parasitic origin. Observations made to determine the viability of the carcinoma cells when subjected to different temperatures, light, etc., showed that positive inoculations could be obtained with isolated portions of the tumor which had been kept at from 1° to 3° C. for eighteen days, and at room temperature for twelve days, while at body heat the tumor cells became inactive after twenty-four hours. At a higher temperature the tissue was rapidly killed. All inoculation experiments were negative with portions of the growth heated for five minutes at 47° C. Intense light likewise proved very destructive to the cells, although it apparently penetrated but a short distance into the pieces of tissue. Partial drying was injurious, and a ¼ per cent. carbolic acid solution caused death of the cells after a period of five minutes.—W. T. L.

The Action of Bacteria on the Hæmoglobin of Blood.—LOBBÉ (*Arch. de méd. exp. et d'anat. pathologique*, 1903, xv. 364) has found that both pathogenic and non-pathogenic bacteria act as reducing agents when grown in contact with hæmoglobin or oxyhæmoglobin. Their action was found to be of two distinct kinds. Gradual reduction and transformation of hæmoglobin into methæmoglobin was apparently caused by secretions from the bacteria, for such reducing substances could be demonstrated in filtered toxins from the bacteria. The nature of the changes in the hæmoglobin varied according to the species of bacterium used, and the substance produced by the bacteria was, therefore, considered as more or less specific. On the other hand, the marked reduction of oxyhæmoglobin into reduced hæmoglobin appeared to

be intimately associated with the life of the organism. This process was brought about by an intracellular combustion, the bacterium absorbing oxygen from the oxyhæmoglobin and thus transforming the latter substance into reduced hæmoglobin. This property should not be considered as specific, but common to all bacteria as well as to all living cells. The author believes that these results offer an explanation for the changes in color of the blood in severe septicæmia, for it appears not improbable that small amounts of methæmoglobin and reduced hæmoglobin may be formed in the body when large numbers of bacteria circulate in the blood. De Ruyter has already found certain spectral bands in the blood from cases of malignant œdema which are nearly identical with the bands formed by methæmoglobin, though they show some minor differences. The formation of methæmoglobin in the blood would ultimately lead to the most important consequences. As more and more hæmoglobin is reduced to methæmoglobin, there would finally result an asphyxia of the cells of the body. Such alteration, according to the author, may be offered as an explanation for the mechanism of death in certain cases of septicæmia where there is no mechanical cause to explain the phenomenon.—W. T. L.

An Improved Method for the Microscopic Diagnosis of Intermittent Fever.—Ross (*Lancet*, 1903, vol. clxiv. p. 86) uses a thick smear of the suspected blood, containing at least twenty times as many corpuscles as the ordinary preparation. When this smear is not fixed, but stained immediately with aqueous eosin, the hæmoglobin is dissolved out, leaving only shadows of red corpuscles. A counterstain of methylene blue brings out the parasites clearly. In cases with a few organisms the time saved by this method of staining is very considerable.—F. P. G.

Bronchopneumonia with Whooping-cough.—JOACHMANN and MOLTRECHT (*Zentralb. f. Bakt.*, 1903, xxxiv. 15), in twenty cases of bronchopneumonia in Eppendorf following whooping-cough, three of which were fatal, found an organism resembling the bacillus of influenza, which they named Bacillus pertussis Eppendorf. This organ was isolated in pure cultures from the lungs of the fatal cases and from the sputum of the other cases in the convulsive stage. The bacillus is regarded as the specific factor in whooping-cough by the writers. It grows only on media containing hæmoglobin, and then with difficulty and as discrete colonies.—F. P. G.

On the So-called Invisible Microbes.—ROUX (*Bull. Pasteur*, 1903, i. 7 and 49) says that as early as 1881 Pasteur suggested that rabies might be due to a microbe which was so small as to be invisible in ordinary microscopic preparations. Since 1898 several diseases have been studied, some of which are unquestionably due to microbes too small to be within the limits of the present-day microscope. Among these may be mentioned "aphthous fever," "peripneumonia of cattle," "horse sickness," "bird pest," "cattle pest," "yellow fever," and "sheep rot." Serum from animals dead of any of these diseases will, when diluted and passed through Chamberlain bougies, give a filtrate which, while free from visible organisms, may show a slight cloud in

bouillon cultures, and will in each case produce the typical disease. In the case of peripneumonia of cattle, by giving the organism intraperitoneally in collodium sacs, it has been possible to bring it to a size that is just visible with the highest power of the microscope. Small colonies of the same organism were grown on a special agar medium.

The problem in connection with these small organisms seems to lie in the line of the discovery of media suitable for demonstration of growth. The probability of the further perfection of the microscope is doubtful, but microphotography may avail somewhat in the settling of these questions.—F. P. G.

Pemphigus Vegetans.—HAMBURGER and RUBEL (*Bulletin of the Johns Hopkins Hospital*, 1903, xiv. 63) review the somewhat confusing literature relating to the varieties of pemphigus and report a fatal case of the form known as p. vegetans. The mouth and almost the entire body of the patient were covered with bullous eruptions and excoriations. At autopsy a firm, nodular, white mass was found in the anterior mediastinum which consisted of lymphoid connective tissue. The organs otherwise were normal. Cultures from the mouth and the heart's blood gave pure growths of a small bacillus which seems to belong to the pseudodiphtheria group. This organism is pathogenic for rabbits and guinea-pigs when injected subcutaneously, and is regarded by the writers as the etiological factor in the production of the disease.

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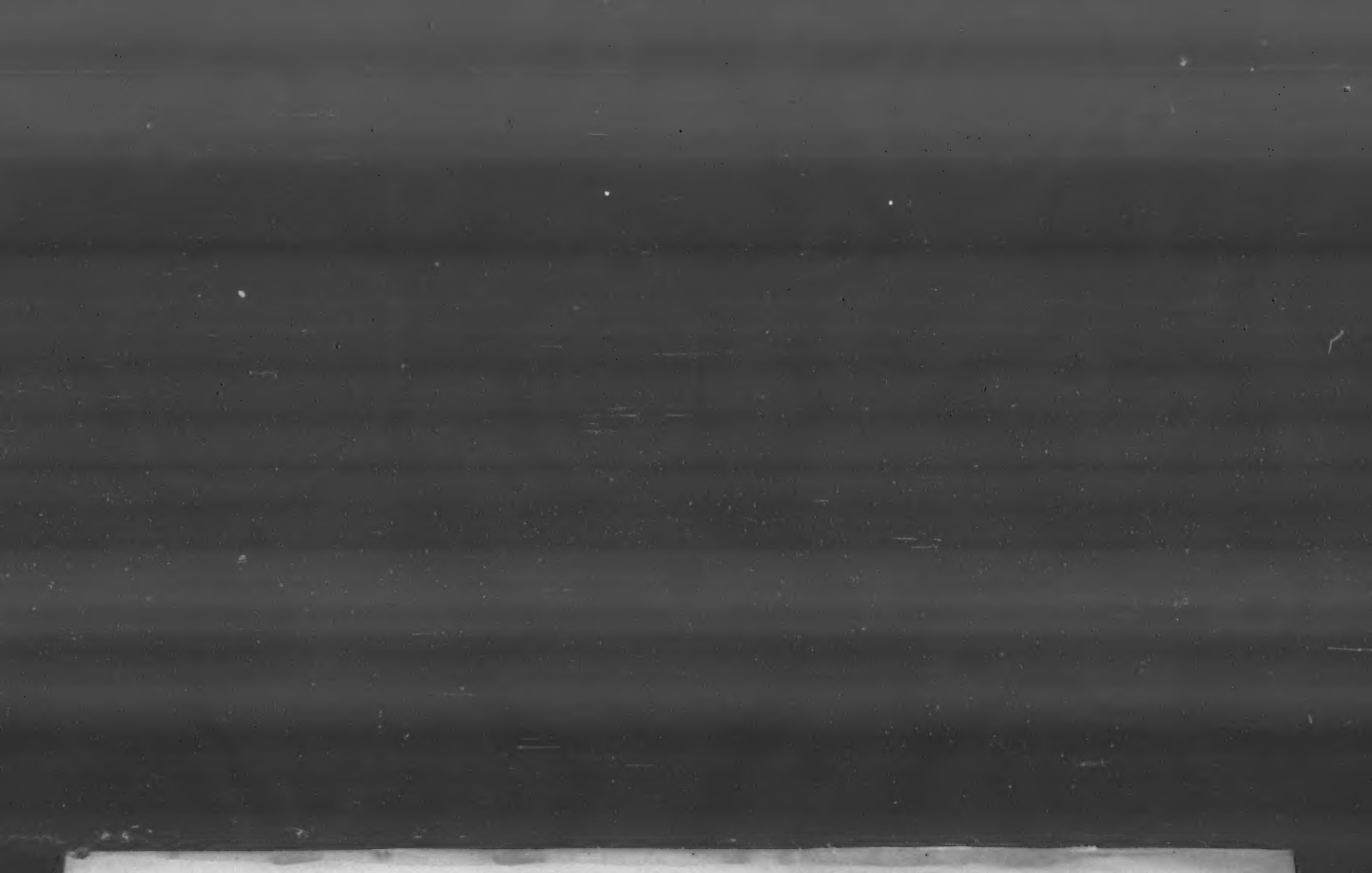

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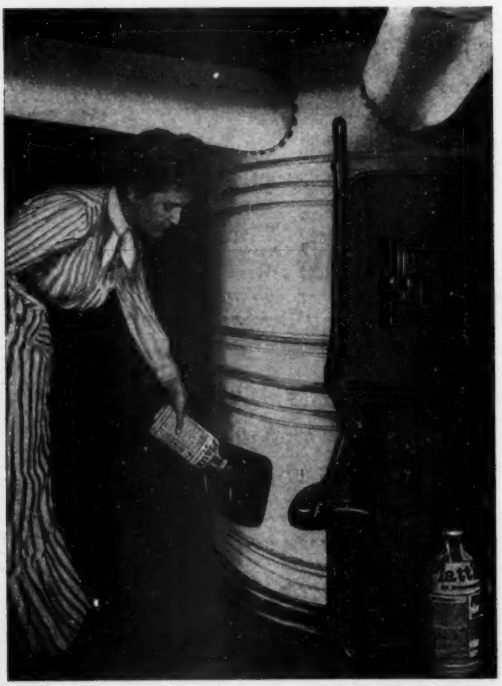

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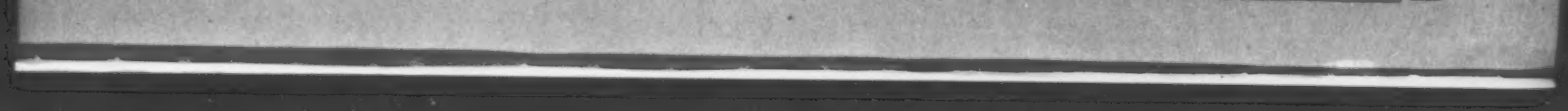

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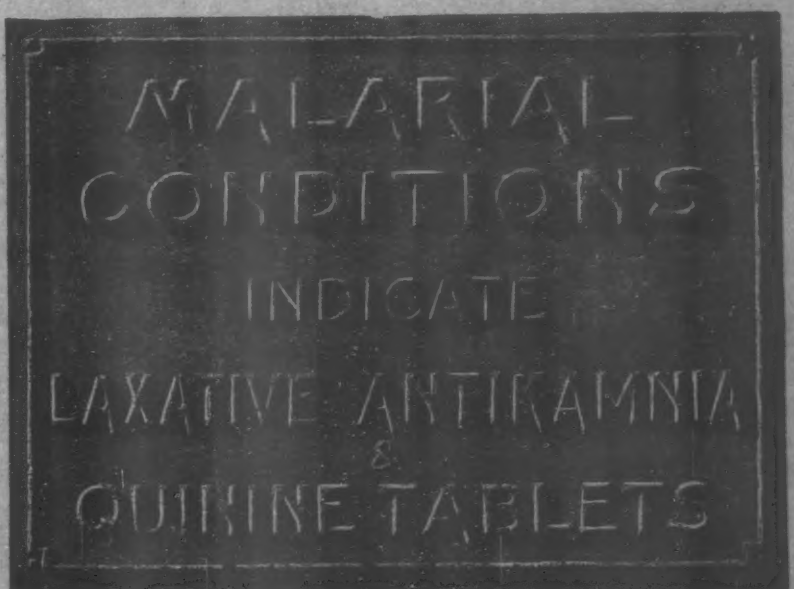

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